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Contents

On the Angle of the Anterior Chamber and the Aqueous Vein in Acute Glaucoma ..... *Norishige Ogino*

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3

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VOLUME 1. October~December 1957. NUMBER 3.

Contents

On the Angle of the Anterior Chamber and the Aqueous Vein in Acute Glaucoma ..... *Norishige Ogino* ... 171

The Statistical Observation on the Outpatients at the Clinic of Ophthalmology, School of Medicine, University of Tokyo ..... *Yukio Uchida* ... 179

Studies on the Genetic Mechanism of Myopia ..... *Toshiyuki Furusho* ... 185

Studies on the Vascular Architecture of the Eye ..... *Hiroo Obara* ... 190

Clinical Application of Electro-Oculogram ..... *Makoto Hiroishi* ... 194

Studies on Visual Perception of Moving Objects ..... *Katsutoshi Asahi* ... 199

An Experimental Observation upon Lymphatic Channels in Vitreous, Retina, and Optic Nerve ..... *Yoshimasa Isayama* ... 208

The Significance of the Ocular Changes by the Shock Stimuli ..... *Hiroshi Nakaji* ... 214

An Appearance-rate of the Ring of a Rainbow Tints in Glaucomatous Patients ..... *Sadao Shimizu* ... 221

Studies on the Autonomic Eye Pressure Adjustment Function of Normal Eye. Part II ..... *Goro Akagi* ... 225

On the Interrelationship between the Blood Character and the Ocular Pressure of the Glaucoma Patients ..... *Jihei Kinugasa* ... 233

On thirty-two Craniotomized Cases of Leber's Disease with Reference to its Genetic Probelms ..... *Jo Imachi, Ichizo Yaso, and Shuichi Matsumoto* ... 236

Studies on Antigenicity of Components of Lens ..... *Takashi Mizukawa and Yoshihiro Takagi* ... 244

ON THE ANGLE OF THE ANTERIOR CHAMBER AND THE AQUEOUS VEIN IN ACUTE GLAUCOMA

Norishige OGINO
Yokohama University, School of Medicine

It is generally acknowledged that in the fully established state of acute congestive glaucoma the closure of the anterior chamber is always recognized. But the examination of the case is often thwarted by corneal oedema, in spite of the application of glycerin instillation; even if the angle is sure to close, it will remain to be a matter of discussion whether the closure is primary or not; nor is it allowed to observe the aqueous vein owing to excessive hyperemia. So the observation in the early stage of the attack is essential in the study of congestive glaucoma. The purpose of this reports is to study the chamber angle of congestive glaucoma in the early stage of the elevation of ocular tension in relation to the flow of the aqueous.

Method of Examination

In my examination of the aqueous veins a slitlamp microscope with ca. 20 magnifications with the slit widely open was used; and the glass rod phenomenon was always observed. When hyperemia appeared by repeated tonometry and gonioscopy, instillation of diluted adrenalin was applied so that the aqueous vein could be examined during the diminution of the excess blood current. As the purpose of this study lies in examining the conspicuous changes of the aqueous vein, the instillation does not confound the results. Gonioscopy was performed by a gonioprism, sometimes by a Koeppe-type contact lens and a hand-held gonioscope. As schaffer and Tour say, a narrow chamber angle is usually more easily examined by the Koeppe-type lens than by the gonioprism, but the latter was prefered because on-and-off test by Smith was more exactly done by it.

Case Reports

Early cases of congestive glaucoma, which have normal ocular tension and no remarkable changes of vision, and visual field, or those that have a history of doubtful glaucoma attack, and the apparent normal eye in the unilateral acute congestive glaucoma were selected. In these eyes the aqueous vein and the anterior chamber angle were previously examined. In the spontaneous elevation of the ocular tension in the later course or in elevation by means of mydriasis or dark-room test, the aqueous vein and the chamber angle were examined in the course of variation of ocular tension in 16 eyes of 14 cases. Examinations were done as repeatedly as possible on the same patient to make sure of the results.

Results

Aqueous vein. In all cases several aqueous veins were found. Their nature was

approximately similar to that of the normal eyes in former reports.

In all cases shown in Fig. 1~17 the flow of the aqueous vein decreased during the elevation of ocular tension. In the aqueous veins the transparent stream decreased, increasing in consequence the blood content in them. As described above, the cases, in which the aqueous veins apparently disappeared with hyperemia by repeated tonometry and gonioscopy, were examined immediately after diluted adrenalin instillation. In this procedure the blood content of the aqueous vein decreased gradually, and the aqueous often reappeared, but in elevated ocular tension the flow of the aqueous was slow and the glass rod phenomenon was as a rule negative, showing undoubtedly the decrease of the aqueous flow.

When the ocular tension fell spontaneously or by instillation of miotics, the change of the appearance of the aqueous veins was entirely opposite. In the aqueous veins a clear stream reappeared, the colour of the blood became light, the velocity of the stream often increased remarkably, and the glass rod phenomenon altered from negative to positive. There were many cases in which the colour of the other small vessels became faint, or the current became granule-like. It suggests the increased content of the aqueous in the anterior ciliary veins.

These changes in the aqueous flow seemed to be more distinct, when the difference of ocular tension between normal and elevated condition was marked and the changes were rapid. Therefore in the positive cases of mydriasis test, and dark-room test examined from the beginning of the elevation of ocular tension, the variation of aqueous flow was usually distinct, even if the peak of pressure was not so high. Also in the spontaneous elevation of ocular tension the disturbance of the aqueous flow was striking, when a rapid rise had been supposed. On the contrary in rather subacute cases in which the base pressure had markedly risen, the aqueous flow was relatively clearly seen even in the high pressure.

The decrease of the aqueous flow was also evident in acute cases, when the elevated pressure level was high. In cases over 60 mm.Hg the aqueous flow almost disappeared. This was clearly seen in case 1. First in the spontaneous elevation to 76 mm.Hg, (Fig. 1) a thick aqueous vein at the inferior temporal quadrant was filled with blood and no aqueous was seen. After instillation of adrenalin the content of it became almost transparent and the blood sludge remained partly in it, which stagnated and could be moved at will by a glass rod, so the aqueous flow in it was proved to be stopped. In the drop of ocular pressure by miotics, the rapid aqueous flow reappeared. In the mydriasis test of this case, the tension rose to 48 mm.Hg and lowered spontaneously. At this time the aqueous flow decreased, but did not disappear completely, and the closure of the chamber angle remained partial (Fig. 2). Other cases in which the acute and high elevation of ocular tension was seen, also showed a remarkable disturbance of the aqueous flow without exception.

In negative cases of mydriasis test or dark-room test repeated in the suspicious

congestive glaucoma, the obstruction of the aqueous flow was not seen.

Chamber angle. The chamber angle was characteristically narrow in the majority of the cases in normal ocular tension. The corneoscleral trabeculae were hardly seen into the inner part. The ciliary zone was rarely seen. The upper part was especially narrow or closed in most cases. The part direct below was occasionally very narrow, but usually the part beneath the temporal and beneath the nasal part were relatively wider.

The chamber angle was completely closed in most cases of elevated intraocular pressure, especially in over 60 mm.Hg.

In cases of a positive mydriasis test closure of the angle was evident, because light reflex did not occur, on the contrary in most cases of dark-room test and moderate spontaneous elevation, the closure of the angle was presumed by means of the on-and-off test of Smith.

In acute congestive glaucoma the closure of the angle was remarkable, but in subacute cases, it seemed to have a tendency of partial closure even in high intraocular pressure. It was noticeable that frequently the elevation of ocular tension occurred some time after the closure of the angle. In case (Fig. 16) 13, after one hour of the closure of the angle by instillation of neosynesine, the tension was normal but one hour later it suddenly rose. In case 6, (Fig. 8) after repeated instillation of eserine the angle closed by extreme ballooning of the iris root, and one hour later the tension rose to 72 mm.Hg. In case 11, (Fig. 14) the angle almost closed without elevation of the ocular tension by mydriasis. After instillation of eserine the patient left the hospital, and about half an hour later he was attacked by sudden blurring of vision.

In negative cases of mydriasis test the angle was open except two cases. In these two cases ocular tension was normal in spite of theapparent closure of the angle, and the aqueous flow did not change.

In the elevation of the ocular tension even to 90 mm.Hg, hyperemia was not seen except that of repeated tonometry and gonioscopy. In case 13, there was no hyperemia in the tension of 90 mm.Hg in positive mydriasis test, and next morning the eye of the patient showed considerable hyperemia by an acute congestive attack. The hyperemia lasted for a few weeks after the drop of tension by means of miotics.

Discussion

Few reports were published concerning the aqueous vein in acute congestive glaucoma. Thomassen and others reported special cases of simple glaucoma with intimate correlation between the appearance of the aqueous vein and the ocular tension. The aqueous vein was filled with blood during the rising phase of the tension, and was filled with aqueous during the falling phase. But a typical case shown by their report did not seem to be simple glaucoma, even according to their opinion. Although it experienced no acute attack, that case seems to be subacute congestive glaucoma. Dobree described the similar finding in a case in his report on vascular changes of

congestive glaucoma. Including Thomassen's case, he explained, that the pressure elevation was due to the closure of the angle. Smith described also in his report on the chamber angle of congestive glaucoma, a case (case 2), in which the aqueous vein could not be seen in the rising phase and appeared clearly in the falling phase of tension. Kleinert examined the fluorescent aqueous flow by means of injection of fluorescein solution into the anterior chamber illuminating by an ultraviolet source. He discovered the considerably diminished aqueous flow during an acute attack.

My results completely corresponded to these reports. It would be indisputable that in congestive glaucoma the aqueous flow can hardly be found in sudden and strong elevation of ocular tension, and reappears in the descending phase.

Concerning the chamber angle in congestive glaucoma many reports are found.

Barkan first asserted, the chamber angle was usually very narrow even in normal tension. Sugar, Chandler, Francois and Ogino stated a similar view. The narrow chamber angle is considered by these authors as the anatomical configuration which is the primary cause of congestive glaucoma.

On the angle in elevated ocular tension, many authors agreed that the angle was completely closed in an established case. Sugar proved the angle closure and the rise of tension in six cases by means of the mydriasis test performed in twenty cases of narrow angle. Francois saw the angle closure in sixty-one cases of congestive glaucoma, twenty-three of which were acute or subacute, and thirty-eight cases chronic, except one case. Smith examined the initial stage of elevation of ocular tension. He proved the complete closure rarely with usual gonioosopy, but the possible angle closure in some cases by means of on-off technic.

On the contrary, Troncoso reported that in acute and subacute congestive glaucoma, the angle was free in 26%, partially closed in 46%, and completely closed in 26% cases. Weinstein saw the open angle in one case of positive dark-room test. However those results were not complete, because they were obtained without the on-off test.

According to my results, the closure of the angle would be no doubt the cause of pressure elevation in some cases, and the probable cause of the others by on-off test, but subacute cases seemed to have often partially open angle.

The reports on the angle closure in congestive glaucoma were obtained often in established state of acute attack. Also they sometimes mixed up chronic cases. The reexamination would be necessary by both authors, who have supported the theory of the angle closure or not.

Summary and Conclusion

The aqueous vein and the chamber angle were examined in 16 eyes of 14 cases in acute congestive glaucoma, before, during, and after the elevation of ocular tension. The flow of the aqueous vein stopped or decreased considerably in the elevation of ocular tension, and increased markedly while the tension fell. This phenomenon was

very evident when the pressure rise was high and steep, and somewhat indistinct in rather subacute cases. The chamber angle was often completely closed in cases of high pressure elevation. In moderate spontaneous elevation and positive dark-room test, the angle was frequently open in usual gonioscopy, but the angle closure was often presumed by means of on-and-off method.

In all negative cases of mydriasis test or dark-room test, the aqueous vein showed no change, and the chamber angle was open except in three cases. One of the latter cases developed the symptom of an acute attack half an hour after the examination.

The elevation of ocular tension in acute congestive glaucoma seems to be due to the obstruction of the aqueous outflow, and the possible cause of the latter would be the closure of the chamber angle in the majority of cases.

Fig. 1

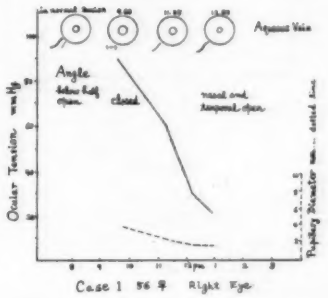


Fig. 2

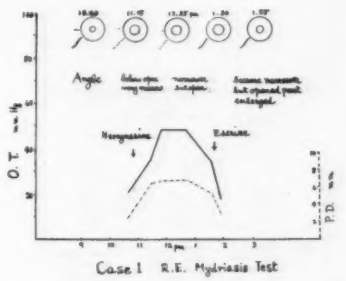


Fig. 3

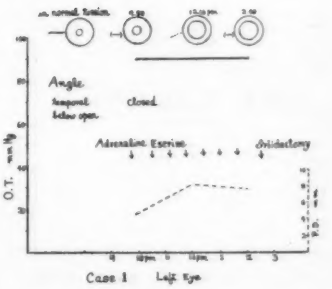


Fig. 4

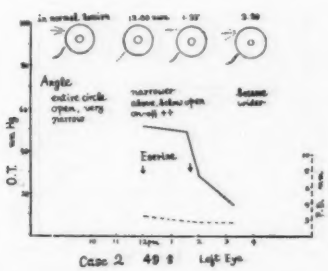
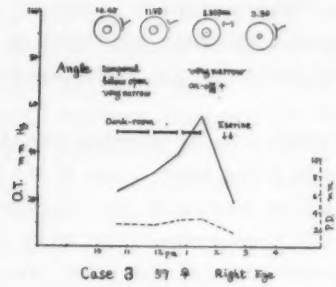
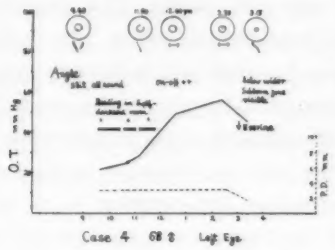


Fig. 5



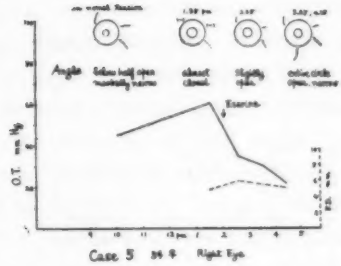
Case 3 57 ♀ Right Eye

Fig. 6



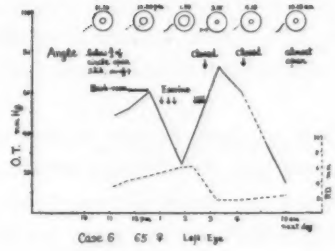
Case 4 68 ♀ Left Eye

Fig. 7



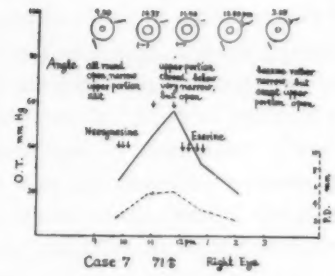
Case 5 56 ♀ Right Eye

Fig. 8



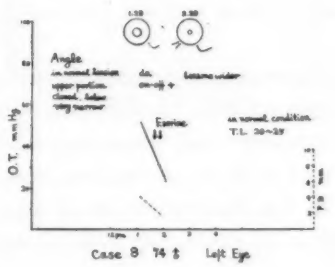
Case 6 65 ♀ Left Eye

Fig. 9



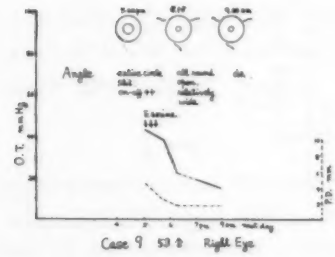
Case 7 71 ♀ Right Eye

Fig. 10



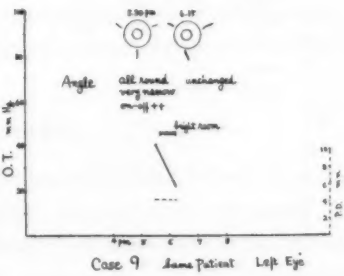
Case 8 74 ♀ Left Eye

Fig. 11



Case 9 53 ♀ Right Eye

Fig. 12



Case 9 Same Patient Left Eye

Fig. 13

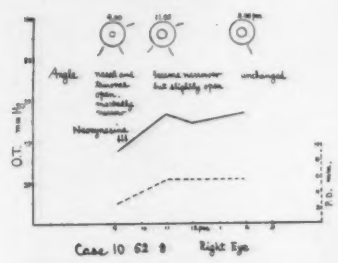


Fig. 14

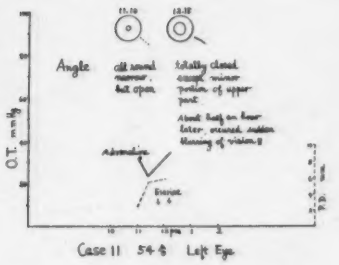


Fig. 15

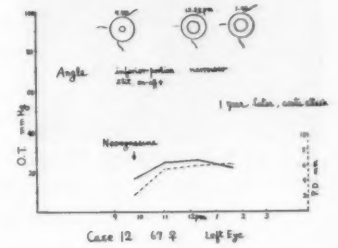


Fig. 16

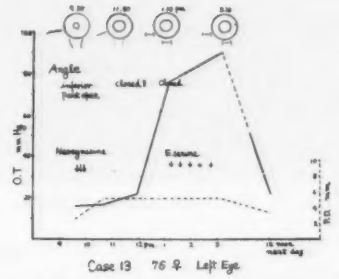


Fig. 17

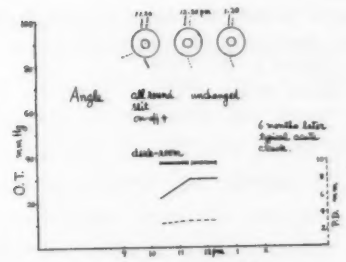
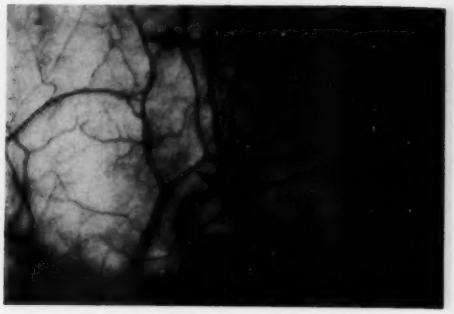
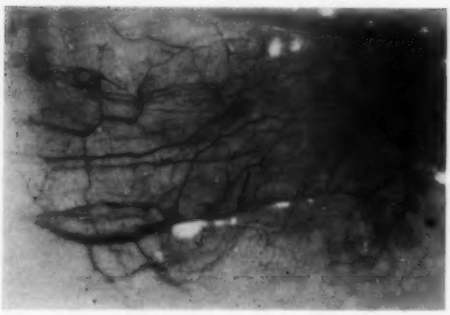


Fig. 18 The aqueous vein in the normal and elevated ocular tension

Case 4 O.T. 22.5mm.Hg, 9.40am



Case 4 O.T. 56mm.Hg, 2.20pm



Case 13 O. T. 15.5mm·Hg, 9.35am

Case 13 O.T. 76mm.Hg, 1.10pm

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THE STATISTICAL OBSERVATIONS ON THE OUTPATIENTS AT THE CLINIC OF OPHTHALMOLOGY, SCHOOL OF MEDICINE, UNIVERSITY OF TOKYO IN 1955

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It is considered that eye diseases are influenced by the changes of social circumstances or environments of life, in their sorts, properties or incidences. These conditions have undergone a considerable transformation at the present, ten years after the end of the war, accompained by notable progress in therapy. In order to recognize these facts, I have performed a statistical study on the outpatients in 1955 and compared the results with those, which had been reported in our clinic in 1924, 1935 and 1942.

In 1955, the total number of outpatients who visited our clinic were 12,882 in which deseased eyes were 19,482. If one eye had two or more independent diseases, they were counted under the respective item. Table 1 shows the number of each case, grouped by its region of the lesion and its percentage to the total number of cases. Diagnosis was forced to be made at their first visits, and enevitably suspected cases were also counted under the same item. Extrme rare cases were omitted from this table.

In Table 2, Mitarai (1924) and Ishihara (1935, 1942) have shown the proportions of the diseased eye in percentage to the eye number of patients. In order to compare the incidences in several diseases, I have followed the same method and shown them in Table 2.

In comparison of the incidences in each year, as the cause of the change of the percentage of the disease, the change of the diagnostic criteria should be considered as well as the advance in therapeutics, social hygiene and prophylactic measures.

Marginal and angular blepharitis have decreased in 1955, whereas hordeolum is found to occur with similar percentage. Chalazion has decreased up to approximately the half of the cases in 1935, but has not shown much difference from that in 1942. Those caused by sequelle of trachoma such as trichiasis and ectropion have decreased considerably.

Dacryocystitis has decreased to half of that in 1942 in incidence.

Acute conjunctivitis has shown a remarkable decrease. Trachoma has followed the trend of decrease on the successive years, as in 1955 being one tenth of that in 1924, whereas chronic conjunctivitis is found four times as much as that in 1935. It seemed to be considerably meaningful, if man thinks that the full blown trachoma accompanied by follicles, scars or pannus has almost disappeared with the advent of antibiotics or advance in prophylactic hygiene, and the group of trachoma of an extremely mild or incomplete form has increased in number. Phlyctenular conjunctivitis has decreased. Recently gonorrheal conjunctivitis has never been found in our clinic.

Table I Survey of frequency of diseases.

$$\% = \frac{\text{Number of each case}}{\text{Total number of cases}} \times 100$$

	No. of cases	%
a) Lids		
Hordeolum	197	1.01
Blepharoconjunctivitis	159	0.82
Entropium ciliarum	143	0.73
Chalazion	132	0.70
Trichiasis	102	0.52
Blepharitis eczematosa	69	0.33
Dermatitis	64	0.29
Ptosis	57	0.29
Blepharitis marginalis	34	0.17
Ectropium palpebrae	22	0.11
Cicatrix	21	0.11
Blepharitis angularis	21	0.11
Lagophthalmus	20	0.10
Tumor palpebrae	19	0.10
Entropium palpebrae	19	0.10
Blepharospasmus	18	0.09
Trauma	17	0.09
Blepharochalasis	11	0.06
total	1.194	6.13
b) Lacrimal apparatus		
Obstructio ducti	114	0.59
Dacryocystitis chronica	63	0.32
Dacryocystittis acuta	10	0.05
Tumor glandulae lacrim.	8	0.04
total	210	1,08
c) Conjunctiva		
Conjunctivitis chronica	1.953	10.01
Trachoma	557	2.86
Conjunctivitis acuta	444	2.28
Pterygium	79	0.41
Hyposphagma	78	0.40
Conjunctivitis vernalis	74	0.38
Folliculosis conjunctivae	56	0.29
Phlyctaene conjunctivae	45	0.23
Pinguecula	35	0.18
Infarctus glandulae tarseae	29	0.15
Trauma	23	0.12
Lithiasis conj.	14	0.07
Tumor conj.	9	0.05
Naevus	8	0.04
Xerosis	4	0.02
total	3.486	17.80
d) Cornea		
Nubecula, Macula	556	2.91
Keratitis superficialis diffusa	141	0.72
Trauma	140	0.72
Kerat. superf. punctata	94	0.48
Leucoma adhaerens	80	0.41
Degeneratio corneae	50	0.26
Phlyctaene corneae	47	0.24
Kerat. interstitialis	46	0.24
Pannus trachomatosus	44	0.23

Eroiso corneae	32	0.16
Ulcus corneae	30	0.15
Herpes corneae	30	0.15
Staphyloma	23	0.12
Microcornea	19	0.10
Arcus senilis	14	0.07
Kerat. sclerotica	13	0.07
Keratoconus	8	0.04
Tumor corneae	6	0.03
Ulcus corneae serpens	3	0.02
total	1.440	7.39
e) Sclerotics		
Scleritis	59	0.30
Staphyloma	6	0.03
Trauma	6	0.03
Sclera cerulea	2	0.01
total	79	0.41
f) Iris, Ciliary body		
Iridocyclitis	200	1.02
serosa	41	0.21
fibrinosa	12	0.06
diabetica	17	0.09
tuberculosa	8	0.04
Behçet's	69	0.35
Coloboma iridis	67	0.34
Synechia	64	0.32
Uveitis	29	0.15
Membrana pup. persistens	18	0.09
Trauma	17	0.08
Seclusio pupillae	14	0.07
Hyphaema	9	0.05
Aniridia	7	0.04
total	463	2.38
g) Choroid		
Chorioretinitis centralis	120	0.62
Morbus Haradaii	20	0.10
Coloboma chorioideae	20	0.10
Tuberculosis	16	0.08
Chorioret. disseminata	7	0.04
Chorioret. diffusa	5	0.03
Ruptura chorioideae	4	0.02
total	196	1.01
h) Retina		
Angiosclerosis retinae	1372	7.05
Degeneratio pigmentosa	230	1.17
Atrophia retinae	96	0.49
Amotio retinae	85	0.44
Haemorrhagia retinae	84	0.43
Thrombosis venae	73	0.37
Haemorrhagia ret. et corp. vit. recidiva juvenum	59	0.30
Degeneratio macula lutea	45	0.23
Conus inferior	43	0.21
Fundus hypertonicus	38	0.20
Retinitis proliferans	37	0.19
Retinitis diabetica	27	0.14
Retinitis albuminurica	26	0.13
Fundus albinoticus	22	0.11

Fibrae medullatae ret.	15	0.08
Atrophia mac. luteae	14	0.07
Perforatio mac. luteae	11	0.06
Ablatio falciform. cong.	10	0.05
Glioma ret.	10	0.05
Retinitis striata	9	0.05
Retinitis exsudativa	8	0.04
Embolia art. cent.	7	0.04
Morbus Takayasui	7	0.04
Commotio ret.	6	0.03
Morbus Oguchii	4	0.02
total	2.407	12.40
i) Vitreous		
Myodesopsia phisiologica	122	0.63
Opacitas corporis vitrei	111	0.57
Haemorrhagia c. vit.	53	0.27
Ablatio c. vit.	25	0.13
Arteria hyaloidea persist.	9	0.05
Synchisis scintillans	8	0.04
total	331	1.70
j) Optic nerve		
Atrophia nervi optici	226	1.16
simplex	90	0.46
neuritica	17	0.09
axialis	12	0.06
Papilla oedematosa	150	0.77
Neuritis	90	0.46
retrobulbaris	46	0.24
axialis	15	0.08
papillitis	11	0.06
Pseudoneuritis	42	0.22
Colobom nervi optici	10	0.05
total	331	1.70
k) Lens		
Cataracta senilis	873	4.48
C. congenita	135	0.69
C. complicata	97	0.50
C. traumatica	57	0.29
C. residua	47	0.24
C. diabetica	13	0.07
Luxatio lentis	13	0.07
Aphacia	97	0.50
total	1.386	7.12
l) Eyeball, Orbit		
Phthisis bulbi	88	0.45
Anophthalmus	56	0.29
Microphthalmus	53	0.27
Exophthalmus	44	0.23
Tumor orbitae	17	0.09
Iron foreign body	7	0.04
Panophthalmitis	7	0.04
Ophthalmia sympathica	4	0.02
Siderosis	2	0.01
Cellulitis orbitalis	1	0.01
total	302	1.56
m) Glaucoma		
Glaucoma primarium	216	1.11

G. secundarium	55	0.28
G. absolutum	29	0.15
Buphthalmus	43	0.22
total	343	17.6
n) Refraction, Accommodation		
Myopia	2.945	15.11
Hyperopia	606	3.11
Astigmatismus	1.162	5.96
myopicus	928	4.47
hyperopicus	87	0.45
Presbiopia	466	2.39
total	5.288	27.1
o) Motility		
Strabismus concomitans	411	2.10
Nystagmus	222	1.14
Heterophoria	134	0.69
St. paralyticus	119	0.61
Myasthenia	27	0.14
total	249	4.87
p) Misc.		
Asthenopia	478	2.46
Amblyopia	120	0.62
Scotoma scintillans	74	0.38
Color blindness	82	0.42
total	876	4.50

Table 2 Comparison of the percentages of several diseases in 1955 with those in 1924, 1935 and 1942

$$\% = \frac{\text{Number of each case}}{\text{Total number of patients} \times 2} \times 100$$

	1924	1935	1942	1955
Blepharitis marginalis	3.49	2.67	1.81	0.49
Belph. angularis	2.59	0.47	0.52	0.10
Hordeolum	1.20	1.01	0.97	0.92
Chalazion	1.43	1.29	0.67	0.62
Trichiasis	3.14	1.77	1.04	0.48
Dacryocystitis	0.98	0.71	0.70	0.34
Obstructio ducti nasolacrim.	0.89	0.66	0.74	0.53
Conjunctivitis acuta	5.85	5.18	8.41	2.07
Conjunctivitis chronica	13.90	2.37	0.23	9.19
Phlyctaene conj.	3.03	1.32	1.42	0.21
Conjunctivitis gonorrhoica	0.23	0.12	0.11	0
Trachoma	27.81	24.52	12.25	2.61
Phlyctaene corneae	2.51	1.37	1.16	0.21
Keratitis interstitialis	1.13	1.08	0.94	0.21
Kerat. superficialis diff.	1.92	3.12	1.01	0.66
Kerat. superf. punctata	0.36	0.36	0.92	0.43
Herpes corneae	0.04	0.04	0.01	0.14
Keratomalacia	0.17	0.10	0.01	0.01
Iridocyclitis	1.23	0.85	0.89	0.94
Scleritis	0.26	0.43	0.23	0.28
Chorioretinitis centralis	0.36	0.58	1.24	0.56
Degeneratio pigment. ret.	0.56	0.51	1.06	1.07
Amotio retinae	0.11	0.35	0.57	0.40
Glioma retinae	0.04	0.03	0.09	0.05
Angiosclerosis retinae	0.08	0.75	1.21	6.42
Thrombosis v. cent. ret.	0.11	0.10	0.08	0.34

Neuritis axialis	1.05	1.16	0.25	0.06
Neuritis retrobulbaris	—	0.09	0.22	0.21
Atrophia n. op. simplex	0.64	0.75	1.01	0.42
Cataracta senilis	1.96	2.45	3.73	4.08
Glaucoma	1.05	1.04	1.41	1.40
Myopia	12.31	13.63	13.93	13.30
Hypermetropia	2.25	4.36	4.42	2.83
Strabismus concomitans	1.85	2.07	2.93	1.82
Asthenopia	3.91	5.18	1.21	2.23
Iron foreign body	—	0.03	0.26	0.03

The cases of interstitial keratitis in 1955 were 46 eyes, 36 of which were syphilitic and 10 were tuberculous. A slight decrease has been shown in diffuse superficial keratitis. Punctate superficial keratitis shows a lower incidence than that in 1942, when there wes said to be the greatest epidemic of it in this country, while it shows higher incidence than that before that time. It could be conceded that corneal herpes has increased, as a disease which can not be cured by chemotherapy or antibiotics.

The percentages of diseases of outer parts of the eye, which I have described so far, were 55.44% in 1935, 44.70% in 1942 and 32.40% in 1955 respectively.

Of the cases of iridocyclitis, those whose classifications were able to be made with methods of routine examination at their first visits, were given in parenthesis in the table. One might be surprised at a high incidence of Behçet's disease, but only 18 patients out of 69 eyes confirmed as Behçet's disease by further examinations.

Central chorioretinitis, often found in this country, has decreased to half of that in 1942 and is the same as that in 1935. A significantly higher incidence of retinal angiosclerosis in this paper is due to the fact that recently the retinal findings have been thought to be of the greatest importance in hypertensive diseases.

Physiologic myodesopsia involved in the diseases of the vitreous body for convenience, is the highest of this group.

It would be due to the increase of chances of examination because of closer connection obtained with internal medicine or neurosurgery than before, that papilledema has increased to some extent just as in the case of retinal angiosclerosis. Those which are diagnosed as axial optic neuritis, which had been thought to be connected with beriberi, have extremely decreased. Any kind of optic atrophy is found to be in the trend of decrease, particularly is this marked in simple atrophy, To-day one meets rarely with tabetic atrophy, the decrease of which keeps pace with other syphilitic eye diseases. Senile cataract has been increasing in number with the years.

Injury caused by fragments of iron has shown approximately the same incidence as that in 1935. Ishihara stated that an increase of this case in 1942 was the result from hard laboring done by unskilled workers in ammunition factories which grew up rapidly during the war time.

Myopia does not show any great change in each year. As presbyopia, only the cases whose complaints were given were counted.

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STUDIES ON THE GENETIC MECHANISM OF SHORT-SIGHTEDNESS

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The opinion that the short-sightedness will depend on short-sighted workings, was supported by many investigators in the past, but with the progress of statistical methods in human genetics, it has been noted that some hereditary constitutions will be connected with the manifestation of myopia. Jablonski (1922), Yamasaki (1926), Sanjo (1934), Kawakami (1934), Hitomi (1939) and Ōtsuki (1947) have maintained its recessive inheritance. While, statistics of Herman (1937) and Aoki (1938) threw some questions on the recessive inheritance and Wold (1949) thought that a dominant inheritance, a recessive inheritance, a sex-linked inheritance and exogenous causes will be connected with it. Kawakami (1949) has assumed that it depends on a dominant gene with a low penetrance. Generally, the manifestation of a hereditary character is influenced by environments. Provided that the constitution of the shortsightedness be hereditary, its manifestation will also be influenced by short-sighted workings and other exogenous factors. Different opinions concerning to the heredity of myopia may be related to the irregular manifestation of a genotype influenced by environments. The author would determine the heredity of the short-sightedness by the statistics of family studies and analyze it by mathematical formulae derived from the standpoint of the genetic equilibrium by Goto (1954) so as to determine the mode of inheritance, the gene frequency and the manifestation rate.

A new classification of the short-sightedness. The short-sightedness has been divided up to the present into four types; the slight degree, the middle degree, the high degree and the highest degree. But, with respect to the boundaries between them, there is no scientific definition, which differ by different ophthalmologists. At first, the author would determine them on strength of genetical or statistical view points. Steiger (1913) maintained that the frequency distribution of indexes of the ocular refraction is a normal curve as in general biological variations. But the studies of Wilbaut (1926) showed that, as it is symmetrical in young children, though it becomes gradually asymmetrical, stretching to high degrees with aging. This asymmetrical distribution has also been ascertained by Scherer(1928), Tron(1929, and Betsch (1929). In Japan, the frequency distributions of indexes of the refraction were studied by many investigators (Nakajima

1938, 1941; Mizukawa and Wada 1939; Yokochi 1940; Ōyama 1940; Ito and Yokochi 1943; Ishigo 1950; Ōkane, Haga and Sato 1950; Taniguchi 1951). The results of these studies have shown that the frequency distribution curve in a population over 15~16 years old consists of three components (Fig. 1, Fig. 2 and Fig. 3); one group (the second group) has a mode between -3D and -4D in dioptry and the other (the third group) lies lower than -6D except one normal group (the first group).

Fig. 1 Frequency distribution curve of dioptry in a population of 15 years old.

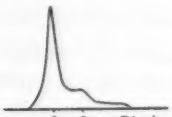


Fig. 2 Frequency distribution curve of dioptry in a population of 16 years old.

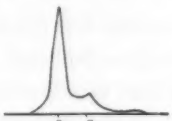
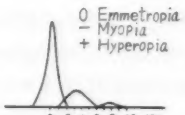


Fig. 3 Three groups decomposed.



From these statistical characteristics, it is assumed that the second and the third groups differ genetically from the first. The author would propose to classify the short-sightedness into two types, the mild type (the second group) and the severe type (the third group), of which the former lies between -2D and -6D and the latter lower than -6D. Many investigators have maintained that the short-sightedness of the high and the highest degrees, of which the most part may be contained in the severe type defined by the author, will be inherited by a recessive gene. Disputations of heredity and environments and of the mode of inheritance up to the present have been connected mainly to this mild type. The study by the author will also be pointed at this mild type.

Observed statistic. The author studied 430 families picked at random from mainly high school students in Kumamoto district, of which the severe types were excluded.

1) Frequency of the short-sighted in the population.

The rate was 13.8 per cent in 1685 individuals tested. As shown in Table 1, the rate increases with age and reaches a maximum at about 16 years old. For the purpose of genetical studies, therefore, children younger than 15 years old should be excluded. There is a difference between the rate in the male (23 per cent) and that in the female (16 per cent), which is nearly significant.

2) Rate of the short-sighted in family studies.

After the exclusion of children younger than 15 years, 365 families remained who were used for the genetical purpose. The statistical data are given in Table 2. Denote the rate of the short-sighted among children from matings of normal×normal by X, that of normal×short-sighted by Y, that of short-sighted×short-sighted by Z, that

Table 1 The frequency of the short-sighted in the population

Age in years	Males			Females		
	Number	No. of myopic individuals	Rate of myopia (%)	Number	No. of myopic individuals	Rate of myopia (%)
1～5	17	0	0.00	16	0	0.00
6～10	156	2	1.28	119	0	0.00
11～15	374	55	14.70	228	13	5.70
16～20	336	81	24.10	152	28	18.42
21～25	121	30	24.79	91	11	12.08
26～30	39	7	17.94	19	2	10.52
over 31	11	2	18.18	6	2	33.33
Total	1054	117	16.79	631	56	8.87
over 16	507	120	23.66	268	43	16.04

Table 2 Statistics of family studies

Combination of parents	Number of families	Number of children	Number of myopic children
Normal×Normal	246	561	74
Normal×Myopia	101	180	67
Myopia×Myopia	18	34	22
Total	365	775	163

Table 3 Rate of the short-sighted in different groups of family studies

$P = 0.1876 \pm 0.0144$
$X = 0.1319 \pm 0.0143$
$Y = 0.3722 \pm 0.0360$
$Z = 0.6470 \pm 0.0812$
$G = 0.2103 \pm 0.0146$

among whole children by G and that among parents by P, then the values are given in Table 3.

Genetical analysis Table 3 shows clearly that the myopia of the mild type or the constitution of it is hereditary. But, if we assume that it is inherited by one recessive gene, the value of Z must be equal to 1.0, and if it is inherited by one dominant gene, the value of X must be zero. Observed values in Table 3 do not harmonize with both assumptions. It is clear that the manifestation of the genotype of myopia will be influenced by environmental factors such as short-sighted workings.

A) Recessive inheritance.

1) The case, in which the short-sightedness is inherited by a recessive gene, and a part of homozygous recessives manifests the short-sightedness. Theoretical formulae of the rates of the short-sighted among different groups in this case are as follows:

$$P = \alpha_a q^2$$
$$X = \frac{\alpha_b q^2 (p+\beta_a q)^2}{(1-\alpha_a q^2)^2}$$
$$Y = \frac{\alpha_b q (p+\beta_a q)}{1-\alpha_a q^2}$$
$$Z = \alpha_b$$
$$G = \alpha_b q^2$$

P,X,Y,Z, and G are the same as those defined in the preceding section. q is the frequency of the recessive gene (the gene of short-sightedness), $p=1-q$, α_a is the manifestation rate of the homozygous recessives in the parents, α_b is that in the children and $\beta_a=1=\alpha_a$. By using these formulae, the values in Table 3 were analyzed to the results that $q^2=0.32$, $\alpha_a=0.59$ and $\alpha_b=0.65$, at which the theoretical values most approaching the observed ones were obtained, as shown in Table 4. q^2 is the rate of the homozygous recessives, i.e., individuals with the constitution of short-sightedness in the population. From this table, it is recognized that the deviations in P,X,Z and G

Table 4 Observed and theoretical values of the rates of the short-sighted

	P	X	Y	Z	G
Observed values	0.1876	0.1319	0.3722	0.6470	0.2103
Theoretical values	0.1888	0.1401	0.3018	0.6500	0.2080
Deviations |d|	0.0012	0.0082	0.0704	0.0030	0.0023
|d|/m	0.0833	0.5734	1.9555	0.0369	0.1575

m is the standard error of the observed value. The deviation is given in its absolute value |d|.

do not exceed the standard errors of the observed values. The deviation of Y is somewhat large but it does not exceed two times of the standard error.

2) The case, in which all of homozygous recessives and a part of the homozygous dominants and the heterozygotes manifest the short-sightedness (i.e., a case of phenocopy). In this case, the deviations are larger than the upper case, giving no satisfactory results.

B) Dominant inheritance.

1) The case, in which all of the homozygous dominants and the heterozygotes, and a part of the homozygous recessives manifest the short-sightedness (i.e., a case of phenocopy). Theoretical formulae in this case are as follows:

$$P = 1-\alpha_a q^2$$
$$X = 1-\alpha_b$$
$$Y = 1-\frac{\alpha_b q (p+\beta_a q)}{1-\alpha_a q^2}$$
$$Z = 1-\frac{\alpha_b q^2 (p+\beta_a q)^2}{(1-\alpha_a q^2)^2}$$
$$G = 1-\alpha_b q^2$$

p is the frequency of the dominant gene (the gene of short-sightedness), q $(=1-p)$ is that of the recessive allelomorph, β_a is the manifestation rate of the homozygous

recessives in the parents, β_b is that in the children, $\alpha_a=1-\beta_a$ and $\alpha_b=1-\beta_b$. Analyzing the values in Table 3 by these formulae, we obtained $q^2=0.90$ ($p^2+2pq=0.10$), $\alpha_a=0.90$ ($\beta_a=0.10$) and $\alpha_b=0.87$ ($\beta_b=0.13$). The theoretical values and the observed ones are given in the Table 5.

Table 5 Observed and theoretical values of the rates of the short-sighted

	P	X	Y	Z	G
Observed values	0.1876	0.1319	0.3722	0.6470	0.2103
Theoretical values	0.1900	0.1300	0.2319	0.3220	0.2170
Deviations |d|	0.0024	0.0019	0.1403	0.3250	0.0067
|d|/m	0.1666	0.1328	3.8927	4.0024	0.4589

2) The case, in which a part of the homozygous dominants and the heterozygotes manifests the short-sightedness. In this case, no satisfactory results were obtained, showing larger deviations than the upper case.

Discussions

Dioptry of the eye will depend on the curvature of the cornea, the focal length of the lens and the length of the ocular axis. It is well known that the corneal curvatures show a normal distribution (Steiger 1913). It has been detected also that, the frequency distribution of the focal lengths of lenses is almost normal, while that of the lengths of the ocular axes show an asymmetrical curve similar to that of the ocular refractions (Stenström 1946, Ōtsuka 1951 a.o.). Therefore, it is assumed that abnormal ocular refractions causing the short-sightedness depend mainly on the long ocular axes. If the short-sightedness is due to this single cause, it is not irrational to assume one gene for its inheritance.

Under the assumption of one recessive gene, a result was obtained, which has been shown in Table 4. The assumption of one dominant gene gave a result shown in Table 5. Comparing these two results, it is clear that the former gives the theoretical values with less deviations from the observed values than those of the latter. Therefore, it is clear that the latter assumption should be abandoned. The former is a case of low penetrance and the latter is that of so-called phenocopy. Judging from Fig. 3, the short-sighted of the mild type will contain no individuals of the homozygous dominants and the heterozygotes (the first group) and exclude a part of the homozygous recessives. Therefore, the assumption of the former case is thought to be correct also by the frequency distribution. In this case, the frequency of the short-sighted in the population must not exceed 32 per cent ($=q^2$). According to many statistics in Japan however, the frequency among students of higher schools, especially of colleges, is over 50 per cent. It is assumed that in the population working customary at the short-sight, all of the homozygous recessives and also a part of the homozygous dominants and the heterozygotes

may manifest the phenocopic short-sightedness.

Summary

By a mathematical analysis based on the genetic equilibrium, it was confirmed that the constitution of the short-sightedness is inherited by an autosomal recessive gene and a part of the homozygous recessives manifests the short-sightedness. The frequency of the homozygous recessives in the population is 0.32. The manifestation rate among individuals of this genotype is 0.65 in the generation of children over 16 years old and 0.59 in the generation of parents.

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STUDIES ON THE VASCULAR ARCHITECTURE OF THE EYE. VASCULAR ARCHITECTURE OF THE CHOROID

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The author investigated the vascular architecture of the choroid, making the vascular cast specimens by plastic injection into the blood vessels of the bulbus, both of the human and grown rabbit.

Results

Results of the rabbits. It is possible for vascular architecture of the choroid to divide into the anterior and posterior vascular zone.

1) General view of the vascular zone.

A) Arterial system.

Aa. iridis which ramify from A. ophthalmica inferior shift to Aa. chorioides, making still finer ramification.

On the other hand, Aa. iridis form a Circulus arteriosus iridis major at the root of the iris and from there, about 15 recurrent choroidal rami, branch off to the outer side.

Except the anterior pole, the thick veins, which line up densely, straight and in order, leave the bulbus and then join into 4 vortex veins behind it.

B) Venous system

Fig. 1 shows a pattern of venous architecture. Thick veins line up densely, in order and straight, except the anterior pole. Finally they pour into the vortex vein and leave the bulbus, joined into 4 vortex veins.

At the anterior pole, venous architecture differs from the other portion. Thick veins make firm anastomosis, forming a dense mesh and a concentric circle with the limbus.

Capillaries in the ciliary processes gather into the vein which run along the divide of the processes. The veins anastomose with the anterior pole veins in the choroid. Therefore, the pole vein receives abundant venous blood from the iris and choroid. It is significant that a thick and dense venous mesh occupies the position and it is easily understood that the mesh contributes to adapt the amount of blood in the iris and choroid.

2) Capillary vascular zone

The capillary mesh in the choroid is of large form and developed anastomosis at the outside of the vascular zone. The mesh spreads on a plane and forms a capillary board.

Small afferent and efferent vessels in the choroid do not run perpendicularly along the capillary board and shift gradually to artery and vein of the choroid closely connected to the board.

Fig. 2 shows capillary mesh at the triangle adjacent to Aa. iridis. In the rabbits, there are no significant differences in the architecture between arterial and venous capillaries.

The mesh is finest in the area of the posterior pole of the bulbus and the aequatory part along Aa. iridis, viz. the area in which Aa. chorioides densely ramifies, then gradually becomes large alond the meridians. The width of the vessels also increase along the meridians from the posterior to anterior. The form of mesh hole is round at the posterior, and at the anterior it seems oval or rectangular.

Choroidal capillary vessels at the anterior pole which closely adjoin the ciliary body, as Fig. 3, arterioles from Annulus iridis major form a capillary mesh at that part. By these facts, it is testified that capillary connection is present between the ciliary and choroidal vascular system.

Bulbus of the human. Vascular ramification in the choroid divides into the anterior vascular zone and inner capillary zone. The former divided further into the outer large vascular zone and inner medium-sized vascular zone.

1) General view of vascular zone

A. Arterial system

Aa. chorioides which branch from A. ophthalmica ramify more, to about 20 arterioles around the disc. These arterioles run directly along the meridians, centering in the disc, radiatory through its entire girth and form the choroidal capillary zone.

B. Venous system

Choroidal veins concentrically confluence to four regions, median superior, inferior and lateral superior or inferior and form 2 or 3 venous sinuses in each region. From each sinus, a main vein runs down and forms a vortex vein, apart from the outer choroidal zone. The diameter of the vortex vein is about 1.5μ at the beginning.

Fig. 1.

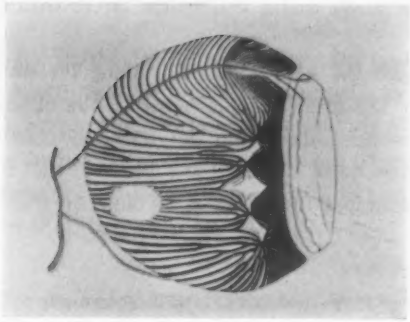


Fig. 2.

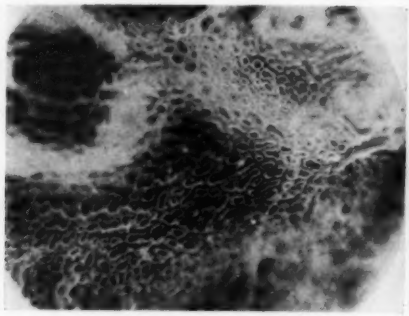


Fig. 3

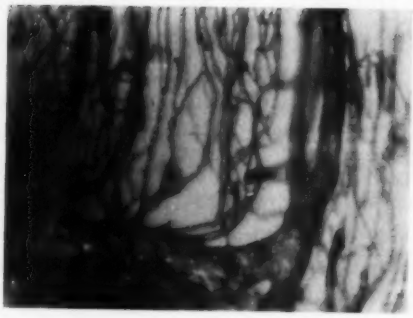


Fig. 4

Fig. 5

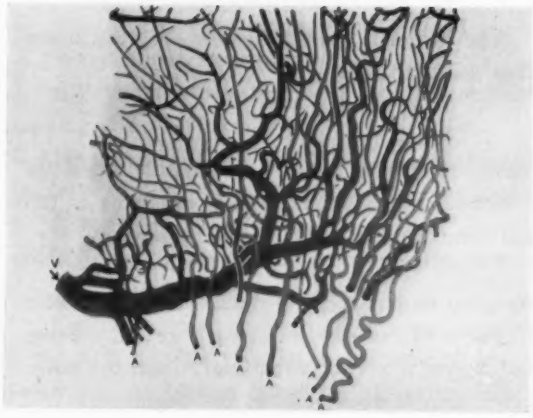
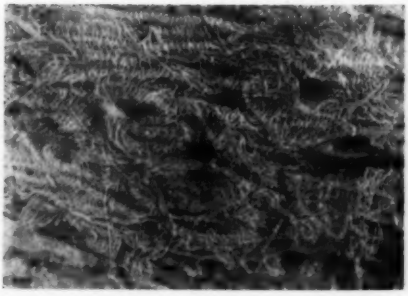


Fig. 6



Centering in the vortex vein, the choroidal vein radiately spread to the papillary and ciliary side. Among them, the meridian veins from each sinus make a dense anastomosis at the posterior pole. On the other hand, the choroidal vascular zone, among the beginning of the vortex vein, shows coarse ramification as in Fig. 5 and form a large vascular zone full of crevices. At that portion, the veins ramify into many small venules. They form many layers, so-called media vascular zone, passing through a very irregular course. At parts, the vascular ramification is so coarse that capillary branches are directly visible from outside. However, the courses of choroidal arteries regularly run on the meridians. 2 different phases of the vascular zone are alterately observed on the meridian of the choroid. One has large vessels, the other is in lack of them. The former shows dense anastomosis at the posterior pole.

2) Capillary zone

Arteries branch off at the choroidal artery and further ramify into small arterioles. The arterioles bend perpendicularly for the capillary zone, directly before they reach it. The capillary mesh created by the arterioles forms a board and spreads on a plane. The vascular architecture is seemingly very complicated, true to the pattern of capillaries.

According to Prof. Kunitomo's classification, they divided into arterioles, prearteriolar capillaries, arterial capillaries and venules. As the results, it is understood that they ramify comparatively regularly, as Fig. 7. However, these types of anastomosis slightly differ from the conjunctival and retinal vessels, viz. when perpendicular arterioles reach the capillary lamina, they immediately ramify into many prearterial capillaries, contributing to the formation of capillary lamina. They form an arterial capillary mesh, causing further ramification and anastomosis. The arterial capillary mesh naturally shifts to the venous capillary mesh. The construction and ramification of the mesh of venous capillaries (common capillaries) are more regular than arterial ones. The major types of ramification in the venous capillary mesh is divided in two.

1. Venous capillaries confluence to a venule from all around on the same plane. The type of concentration shows beautiful rosettes.

2. Venous capillaries confluence into a venule and the type of concentration shows an Indian fan.

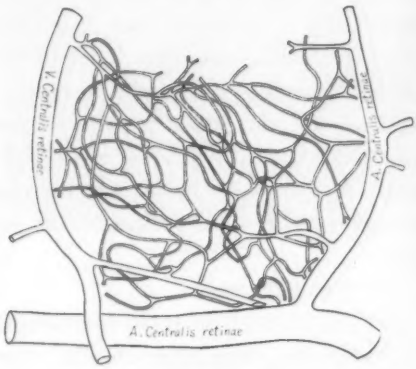
At the posterior pole, the mesh is fine and the diameter of vessels is small. With the distance from the pole, the mesh becomes rough and the diameter increases. At the jaggy margin, the mesh and diameter reach their maximum. Consequently, the posterior pole has a very dense mesh per square. In some part, the type of the mesh is round and it changes gradually to long spindle shape with the distance from the posterior pole.

Fig. 8 shows a pattern of retinal capillaries at the equatorial region which corresponds to Fig. 6 and Fig. 7. In this Fig., the diameter is very poor compared to

the choroidal mesh and anastomosis isvery poor. Consequently, comparatively large mesh is formed. At parts, 2 or 3 vascular zones are piled up.

Fig. 7

Fig. 8



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CLINICAL APPLICATION OF ELECTRO-OCULOGRAM (E.O.G.)

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The most important factors to perform the operation of strabismus are to know, what muscle should be operated on and how much be receded or resected. Of course, the strong muscle must be receded and the weak one must be resected or advanced.

Since the area of the fixation field is determined not only by the power of the agonist but also their antagonist and check ligament, it is better to know the degree of the acceleration in the saccadic eye-movement than to know the limitation of the duction, i. e., area of the fixation field, to measure the power of the extraocular muscle. In the saccadic eyemovement the subject cannot change its velocity or acceleration voluntarily[4,] and the acceleration of the moderate angle eyemovement is controlled by the agonist mainly.

In order to estimate more accurately the power of the ocular muscle, electro-oculography was applied to diagnose the strabismus.

Methode of Electro-Oculography. The face of the subject is fixed in a frame, two electrodes are placed on the nasal and temporal angles of both eyes (horizontal leading) and the one eye is coverd by an occluder, and the subject shall move his eye with the flashing neon-tubes alternately, located on the tangent scale, three feet distant from the subject.

The changes of the corneo-retinal potentials are induced with these two electrodes, amplified with D.C. amplifier[1], and recorded on the ink-writing oscillograph. Further, the amplified signals are electrically differentiated, i. e., the velocity of the eye-movement[2,6], and recorded on the same oscillograph (Fig. 1).

Fig. 1

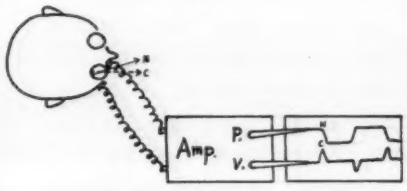
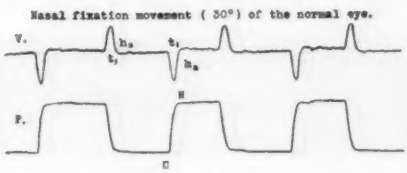


Fig. 2



E.O.G. of the Normal Eyemovement. There are lineal relations between the deviation angle of the eye and the changes of the static potential[3,5]. Average potentials from the primary position to 40 degrees are about 1.0 mV toward the temporal, 0.8 mV to nasal, 0.6 mV to upward and 0.4 mV to downward.

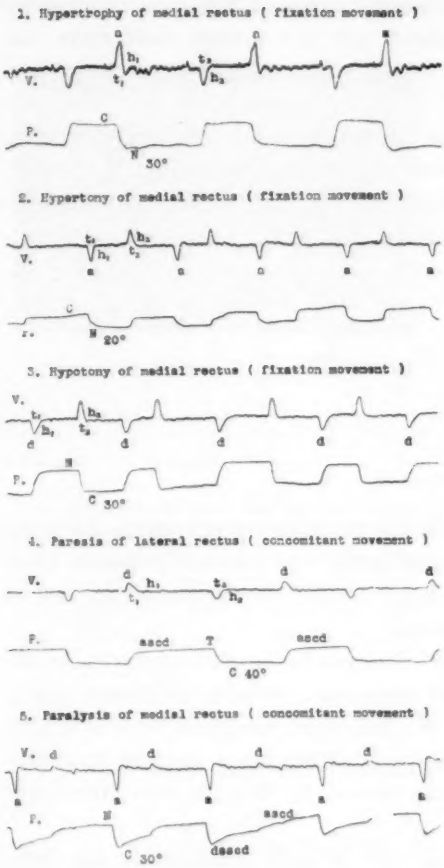
Figure 2 is normal horizontal eyemovement. Changes in the static potential of the non-coverd eye and covered eye are equal at all directions. Velocity is almost nearly constant (about 10 rad/sec[3,]), but the time of centrifugal movement (t_1) is a little longer than that of the centripetal movement (t_2), the difference of them is less than 0.03 sec. in 40 degrees, and the height of velocity curves (h_1) is equal or a little lower than that of the centripetal velocity (h_2).

In eyemovements under 30 degrees from the primary position, it has been observed that there are no differences in the forms of velocity curves between the centrifugal and centripetal movement, and these isoceles velocity curves are called by the name of "uniform-type". But in centrifugal movement above 30 degrees, velocity curves are trnsformed by the action of the antagonist, chek ligaments and others. These scalene velocity curves are called by the name of "decrease-type".

E.O.G. of the Abnormal Eyemovement. In the diagnosis by E.O.G., the true concomitancy was very few in almost all cases even, though they were decided as concomitant strabismus clinically.

Ascending or descending curves in the position records and elongated decrease-types in the velocity records were observed in the cases of atrophy or paresis of some muscle, i. e., an underaction type of strabismus. (Fig. 3-3 to 5) On the contrary, the increase-types in the velocity were observed in the cases of hypertrophy and spasm,

Fig. 3



i. e., an overaction type of strabismus. (Fig. 3-1 and 2) These abnormal curves were observed when the affected eye was executing the fixation movemet, but they were indistinct when the eye was in concomitant movement: because, if the affected and abnormally deviated eye was asked to fixate at the primary position, each muscle should have different activities, owing to the chage of the reciprocal innervation, and if this eye were cover and situated at the physiological static position, each muscle should have peculiar activities.

Based on the above-mentioned facts, it is possible to estimatet he degree of muscular obstacles electrically. Five types were characterized as the muscular obstacles in strabismus as follows;

1. Hypertrophy (Hyperplasy) 2. Hypertony (Spasm) 3. Hypotony 4. Paresis (Atrophy, Hypoplasy) 5. Paralysis.

Figure 3-1 is a record of hypertrophy of the medial rectus muscle in fixation movement. On the velocity record, h_1 is taller than h_2, t_1 is shorter than t_2 and a-curve shows the increase-type. These changes were also observed in the concomitant movemeet of this eye.

Figure 3-2 is a record of hypertony of the medial rectus muscle in fixation movement. On the velosity record, h_1 is a little taller than h_2 and a-curve shows the increase-type. These changes had vanished in the concomitant movement of this eye.

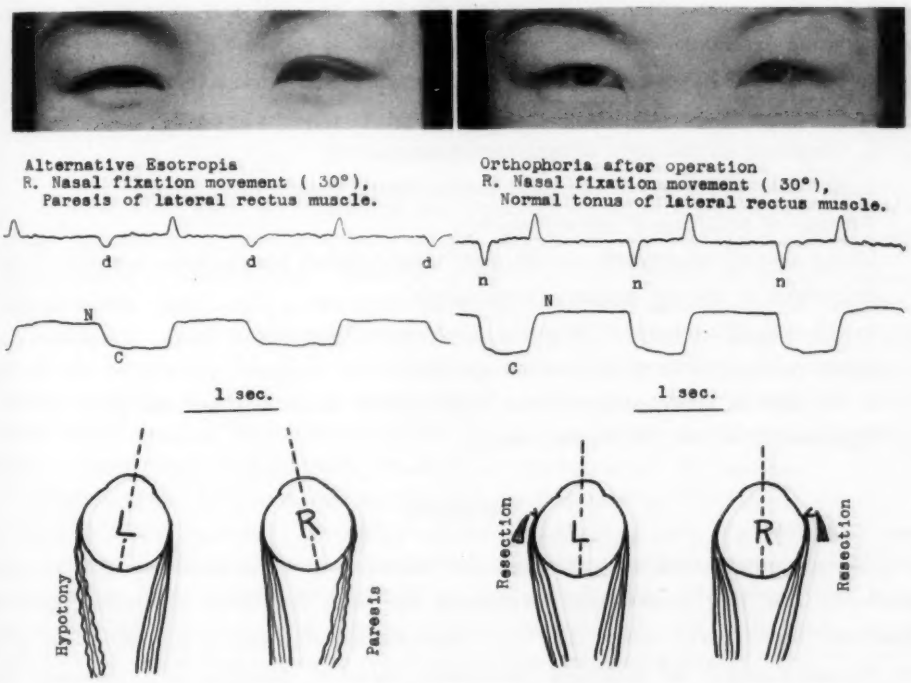
Figure 3-3 is a record of hypotony of the medial rectus muscle in the fixation movement. On the velocity record, h_1 is lower than h_2, t_1 is longer than t_2 and d-curve shows the decrease-type. These changes had vanished in concomitant movement of this eye.

Figure 3-4 is a record of paresis of the lateral rectus muscle in the concomitant movement. In this case, changes in the hypotony are observed more remarkably, and there ascending curves on the position record (ascd) are showon. These ascending curves were observed only in the concomitant movement of theis eye.

Figure 3-5 is a record of the IIIrd nerv palsy in the concomitant movement. In this case, the lateral rectus was the only muscle to rotate the eyeball, and very interesting movement of the paretic eye due to the contraction and relxation of the lateral rectus muscle alone are detectable on the position record, and there ascending and descending curves are shown.

Figure 4 is the record of the pre-and postoperative examinations in an esotropia. On the preoperative record, paresis and hypotony of both lateral recti are shown, but after the resection of them they have regained the normal activities and recovered functionally and cosmetically.

Fig. 4



Practically, concomitant strabismus are classified by the E.O.G. as follows;

Concomitant convergent strabismus
- (1) Paresis of one or both lateral rectus muscle.
- (2) Hypertrophy of one or both medial rectus muscle.
- (3) (1)+(2)
- (4) Anatomical convergent strabismus.

Concomitant divergent strabismus
- (1) Paresis of one or both bedial rectus muscle.
- (2) Hypertrophy of one or both lateral rectus muscle.
- (3) (1)+(2)
- (4) Anatomical divergent strabismus.

It is a well known fact, that if one lateral rectus falls in to paresis, the medial rectus muscle of the other eye will falls into hypertrophy, the lateral rectus of the other eye into atrophy and the direct antagonist into contracture as a secondary muscular change. These changes are indicated very clearly on the electro-oculogram. Futher more, another combination of secondary muscular changes was proved by electro-coulographic experiment, and they were abbreviated as follows,

In the case of hypertrophy of the right medial rectus muscle there occur:

1. Atrophy of the left lateral rectus muscle.
2. Hypotony of the right lateral rectus muscle.

In the case of paresis of the right medial rectus muscle there occur:

Atrophy of both lateral rectus muscles.

In the case of hypertrophy of the right lateral rectus muscle there occur:

Hypertony of the left medial rectus muscle.

In the case of anatomical divergent strabismus there occur:

Hypertrophy of both medial rectus muscles.

In the case of overrecession of the right medial rectus muscle there occur:

Hypertrophy of the left medial rectus.

Summary

The examination of various muscular obstacles in strabismus by E.O.G. were studied. The true concomitant strabismus are very few from the view point of muscular power, even when they are diagnosed as concomitant clinically. In spite of the same length of operation, correction angles of deviation are variously different in most cases of the same kind of concomitant strabismus. Muscles to be operated and their length of attack will be decided more accurately than any other clinical methods of diagnosis. The only inconvenient point to use the E.O.G. is, that it cannot be applied to young children under about six years old, because of the necessity to follow the flashing lamps alternatively. But it will be the most useful method since the power of ocular muscles can be estimated objectively and the subject feels no pain through the measurement.

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STUDIES ON VISUAL PERCEPTION OF MOVING OBJECTS REPORT. 1 VISUAL PERCEPTION OF FLICKERING LIGHT

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In these days when every facet of our daily existence calls for speed, studies on visual perception of moving objects claims importance as one which is inseparable from the life of modern man. As in the cases of studies undertaken by Ludvigh and Hagino on the visual acuity of the fovea during the viewing of moving objects, practically no systematic studies have been made so far. On one hand television has rapidly becoming popularized, various mechanical operations have been calling for movements similar to this, while speed of travel has also continuously been accelerated. Hence when visual function cannot adapt itself to the needs of these ever increasing speeds of visual objects, there will naturally result ocular fatigue and or asthenopia.

Despite these changes in life environment, as has been stated above, studies on visual perception of moving objects are extremely rare. In the present work studies were made firstly on the clarification of the physiological basis underlying, followed by those related to the field of application. As a preliminary step to the study on visual perception of moving objects, experiments were undertaken on the influences of some environmental conditions on the vision of flickering light.

Stueies of f.f.f. have been made by many investigators, and these results have been applied to the clarification of visual physiology, diagnosis, treatment, judgment of prognsios, measurement of fatigue and fatigue causing apparatus. However in the majority of these studies, the test-patches of the flicker were small in size, while the visual distance was short. Contrary to the above, in actual life conditions the objects are, even in the case of television, mostly more than 14 inches, and the small test-patches employed so far cannot be said to be satisfactory enough. Hence experiments were undertaken with apparatus and room described below.

Method

Experimental apparatus. As a test-patch of flickering light, the flicekr apparatus of Hagino & Suzumura was employed. The size of the test-patch of this apparatus is round with a diameter of 38 cm, the time of after glow of the of light source which consisted of a special fluorescent lamp (10W) was 5/100,000 seconds. The range of illumination lay between 30 lx and 150 lx, and was of six grades. The flashes per second could be made to vary from 3 to 180 cycles. The room for experiment was a dark room of 12×3 meters in size, while the control of illumination of the examining room was made by a shadowless illumination apparatus deviced by us and consisting of 320 electric lights attached to the four walls of the examining room. illumination of this apparatus could be adjusted to five strengths by means of a switch. Depending on the conditions required of the experiment an illuminating stand was employed.

With the above apparatus the experimental conditions for visual perception of flickering light consisted of:

1. Illumination intensity of the flickering test-patch, 2. Size of the test-patch,
3. Visual distance, 4. Illumination of the examining room. By various combinations of the above conditions considerations of the influences on f.f.f. were made.

All measurements were made by binocular vision, with natural or artificial pupils. The subjects for examination consisted of 3 males and one female, with no eye diseases.

Experiment I. Effects of changes in size of fest-patch and illumination of the examining room on f.f.f. Experimental Conditions and Results.

Experimental conditions: Visual distance; 50 cm. Illumination intensity of flickering test-pathch; 50 lx (at surface of test-patch). Size of test-patch; visual angles of 1°,10°,25°,40°. Illumination of examining room; dark, 10, 50, 100 and 200lx. In the case of the above the surface of the test-patch was illumimated by the light of the examining room.

Results: As may be seen from Fig. 1, between visual angles of 1° to 10°, as the angle increases f.f.f. rapidly rises, but with the angle of 10° as a limit, subsequent rises become gradual. It thus became clear that a break occurs at a visual angle of 10° as a range. The same picture was noted even when the illumination inrensity of the room was changed. The grade of curvature was found to be the more pronounced the greater the illuminaton intensity of the room. In other words under such a condition the influence of the illumination intensity of the room is extremely samll up to visual angles of 10°, greatest at an angle of 10°, and relatively slight at an angle of 40°. This relationship of size of test-patch to f.f.f. showed the same tendency for changes in visual distances 1 to 5 meters.

Experiment 2. Effects of changes in visual distance and illumination intensity of the exmining room on f.f.f..

1) When the size of the test-patch was kept the same.

Experimental conditions: i. Illumininination intensity of test-patch, 50 lx. Size

Fig. 1. Effects of changes in the size of test-patch and of illumination of the examining room on f.f.f.,
Visual distance; 50cm. Illumination intensity of test-patch; 50lx.

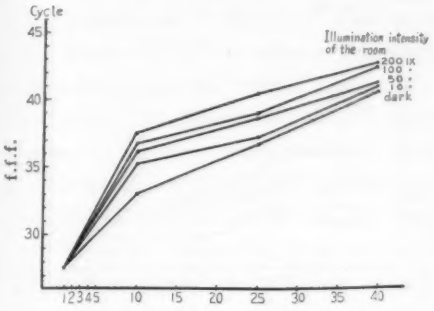
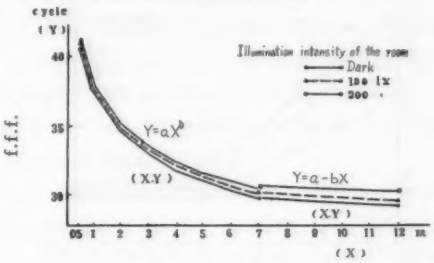


Fig. 2 Effects of changes of visual distance and of illumination intensity of the room on f.f.f., when the size of the test-patch was kept the same. Illumination of the room; only the area surrounding the flickering apparatus was illuminated.
Illumination intensity of test-patch; 50lx.
Diameter of test-patch; 38cm.



of test-patch; kept at a diameter of 38 cm. Visual distance; 50 cm,1 m and increased by one meter to 12 meters. Illumination intensity of room; dark, 100 and 200 lx. In this case an illuminating stand (spot) was employed, and only the area surrounding the flickering apparatus was illuminated.

Experment conditions: ii. With conditions similar to i. the illumination of the examining room was altered, namely, with illumination intensities of 4, 50, 160 and 200 lx, the entire room was illuminated with the previously mentioned apparatus for shadowless illumination of the examining room.

Results: i. As can be seen from Fig. 2, as the distance increased, up to 7 meters, the f.f.f. decreased, but with distances of 8 m and above practically no change was seen. Thus, $Y=aX^b$ for distances of 1-7 m, and $Y=a-bX$ for distances of 7-12 m, where Y = f.f.f., X = visual distance, and a and b constants. As effects of the illumination intensity of the room, when the illumination becomes greater f.f.f. rises with all visual distances.

ii. Under this illumination condition, as may be seen from Fig. 3, with increase in visual distance f.f.f. decreased, and as in the case of i, with 7 m as a limit, $Y=a-bX$ for a distance of 1-7 m, and $Y=a'-b'X$ for distances of 7-12 m, where Y = f.f.f., X = visual distance, and a, b, a', and b' constants. When the illumination intensity was altered, for up to distances of 1-7 m, with increases in intensity of illumination of 4, 50 and 160 lx there was seen a tendency for f.f.f. to increase slightly, but when the intensity became 200 lx there was a contrary fall to a figure less than that for 4 lx. With visual distances of over 7 m the f.f.f. decreased with rise in intensity of illumination.

2) When the visual angle of the test-patch was fixed in accordance with the visual distance.

Fig. 3 Effects of changes in visual distance and of illumination intensity of the room on f.f.f., when the size of the test-patch was kept the same. Illumination of the room; the entire room was illuminated. Illumination intensity of test-patch 50lx, Diamter of test-patch; 38cm.

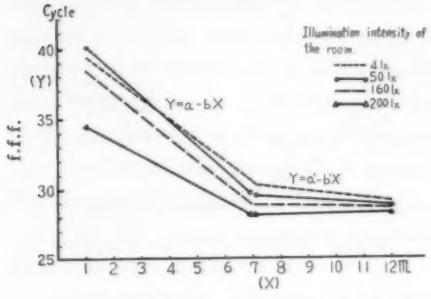
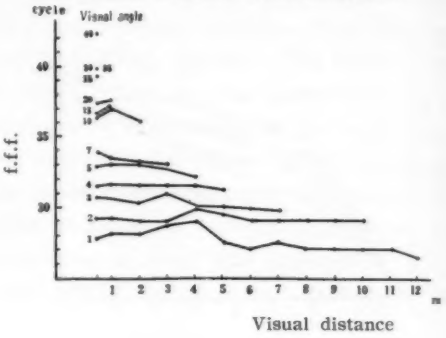


Fig. 4 Effects of changes of visual distance on f.f.f., when the visual angle of the test-patch is the same in each visual distance. Illumination intensity of the room; 10lx. Illumination intensity of test-patch; 50lx.



Experimental conditions: Illumination intensity of test-patch; 10 lx. Size of test-patch; this was altered in accordance with distance, and the visual angles at various distances fixed at 1,2,3,4,5,7,10,15,20,25,30,35, and 40° degrees. Visual distance; same as in Exp. 2.1) i.. Illumination intensity of room; 10 lx.

Results: As may be seen from Fig. 4, when the visual angle remained fixed the f.f.f. decreased only extremely slightly and remained almost the same even when the visual distance was changed. This tendency remained the same even when the illumination intensity of the room was altered.

3) When the size of the test-patch was altered.

Experimental conditions: Illumination intensity of room; dark. Size of test-patch; diameters of 38 cm, 26.8 cm, and 19 cm. Illumination intensity of test-patch and visual distance; same as in 2).

Results: As may be seen from Fig. 5, when the diameter of the test-patch was

Fig. 5 Effects of changes of visual distance on f.f.f. Illumination intensity of test-patch; 50 lx. Illumination intensity of the room; dark., diameter of test-patches; 38, 26. 8, 19cm.

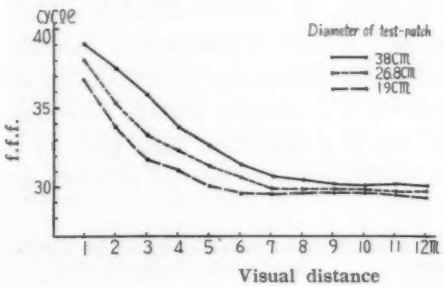
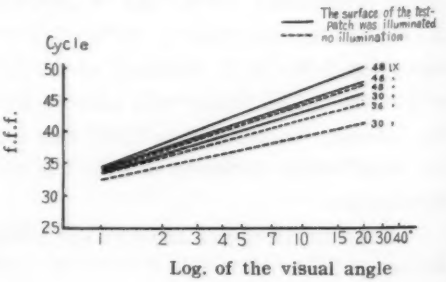


Fig. 6 Effects of illumination intensity of test-patch on f.f.f., Illumination intensity of test-patch; 30, 36, 48 lx. Visual distance; 1m. Visual angle; 1→20°. Illumination intensity of the room; 10 lx.



38 cm, the f.f.f. remained the same at distances of over 7 m as was described above. But with diameter of 26.8 and 19 cm, i. e. when the area of the test-patch was decreasd to 1/2 or 1/4, the f.f.f. remained almost the same for distances of over 7 m and 6 m respectively.

Experiment 3. Effects of illumination intensity of test-patch on f.f.f.

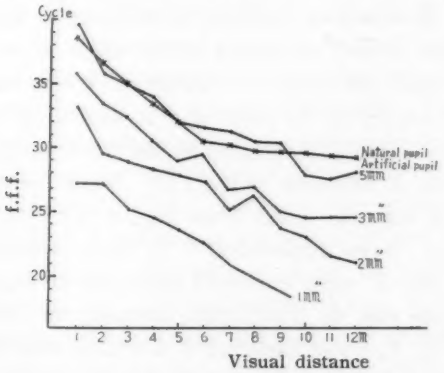
Experimental conditions: Illumination intensity of test-patch; 30, 36, and 48 lx. Size of test-patch; visual angles of 1,2,3,4,5,7,10,15, and 20° degrees. Visual distance; 1 meter. Illumination intensity of room; 10 lx. In this case, by illumination of the room 2 conditions were obtained, namely, 1) where the surface of the test-patch was illuminated, and 2) where a black iron tube of 40 cm was attached infront of the flicker apparatus and the surface of the test-patch was not illuminated.

Results: From Fig. 6, it will be seen that with rise in intensity of illumination of the test-patch the f.f.f. rose, and this rise was seen to be greater the larger the visual angle. If now the logarithm of the visual angle is represented by the ordinate and f.f.f. by the abscissa, with increase in visual angle the f.f.f. was seen to rise in a straight line in cases of illumination of the test-patch by the illuminated light of the room and when not. And f.f.f. was seen to be greater when the surface of the test-patch was illuminated than when not, while grade of increase was greater the bigger the size of the visual angle.

Experiment 4. Effects of the diameter of the pupils on f.f.f.

Experimental condition: Illumination intensity of test-patch; 30 lx. Size of test-patch; 38 cm. Illumination intensity of room; dark. Visual distance; same as in 2,1) ii. Under the above conditions artificial pupils of 1,2,3 and 5 mm were placed infront of both eyes and experiments were undertaken.

Fig. 7 Effects of the diameter of the pupils on f.f.f. Illumination intensity of test-patca; 50 lx. Diameter of test-patch: 38cm. Illumination intesity of the room; dark. Diameter of artificial pupil; 5, 3, 2, 1mm.



Results: As may be seen from Fig. 7, with decrease in diameter of the artificial pupil f.f.f. decrased, while with increase in visual distance there was seen a gradual decrease, unlike the constancy seen in the case of the natural pupil.

Discussion.

With the object and method above described and employing a specially devised flicker, measurements were made by binocular vision, in almost all bases. Thus the results obtained cannot be compared directly with those of other investigators, but considerations will be made of the individual experimental results.

On the visual angle. Many investigations have so far been made on the effects of the visual angle on f.f.f., and the results have more or less coincided. For example Oshima found that f.f.f. became greater with increase in the visual angle. Yonemura, Yamagishi, Granit and Harper and many others stated that f.f.f. rose in proportion to the logarithm of the visual angle. These results with monocular vision were obtained also in the present experiments with binocular vision, and this relationship was seen even when the visual distance was altered, and with changes in illumination intensity of the patch and room.

On the illumination intensity of the room. Regarding the effects of illumination intensity of room on f.f.f. there have been only few reports of experiments made with illumination employed here, and in investigations made so far, for example those of Horiuchi and Yamagishi, many employed an illuminated screen and a flickering test-patch was made to appear at the center. In these experiments it was found that with rise in the surrounding lighting (Horiuchi) there was a regular rise in f.f.f., while Hylkema, Kamiya, Yamagishi, Oshima ann Hashimoto stated that when the illumination intensity of the test-patch was equal to the surrounding lighting f.f.f. reaches a maximum. Schaternikoff and Granit stated that f.f.f. rose greater in cases of light adaptation than in dark adaptation. These experiments differed in many respects from that described here, so that a comparison cannot be made unconditionally. In the experiments here, as was seen in Fig. 1, the effects of illuminating intensity of the room was greatest at a visual angle of 10°, and almost not noted at an angle of 1°. This fact indicates that in the case of visual perception of television, it the visual angle is small the effects of illumination intensity of the room may be said to be slight. Next, when the surface of the test-patch is being illuminated by the illuminating light of the room or when not, there will be a difference in the f.f.f. When the illuminating intensity of the room is 10 lx, as may be noted from Fig. 6, f.f.f. is smaller than when no illumination is employed. From Experiment 2. 1) there appeared a difference when illuminations as in i. and ii. were employed (indicated in Figs. 2 and 3). From Fig. 2 it will be seen that with rise in illumination intensity of the room there resulted a corresponding rise in f.f.f., while from Fig. 3 it will be seen that at visual distances of 1-3 m tfe f.f.f. was at a maximum with a surrounding lighting of 50 lx, falling in the

order of 4, 160 and 200 lx. At distances of 4–12 m it waf greatest with a surrounding lighting of 4 lx, and with rise in surrounding lighting the f.f.f. fell. And the degree of this influence became greater the nearer the visual distance, namely with increase in the visual angle. Thus some effects of the surrounding illumination were noted and it was of interest to find that small changes in environmental condition produced great changes.

On the visual distance. From the aspect of prevention of fatigue resulting from visual perception of moving objects there is great need for considering the visual distance, but literature on this subject is scarce, but this is believed to be due to the difficulty in obtaining large flickering test-patches.

On viewing the results of Experiment 2. 1) i. ii. for distances of 1-7 m, in the case of i. $Y=a\ X^b$, as may be seen form Fig. 3 while in the case of ii. $Y=a-bX$; but for distances of 7-12 m, i. and ii. both show the same process and little change according to distance is observed in f.f.f. That a difference exists between the two when the distance is 1-7 m is believed to be due to difference in the method of illuminating the examining room. Beyond 7 meters both showed the same relationship, and this is due to the fixity of the test-patch so that the visual angle at a distance of 7 m was about 3, and coincides with the findings of Experiment 1. where it was shown that when the visual angle is small the influences of the illumination intensity of the room are slight. That the influences were slight at distances of over 7 m are believed to be due to the effects of the pupils, a finding that will be discussed later. Again, an important factor concerned with the relationship of visual distance and f.f.f. is the visual angle. Compared with the results in Fig. 5 where the sizes of the test-patches were made to vary, at a diameter of 38 cm of the test-patch the f.f.f. decreased rapidly up to a distance of 7 m, as was described before, but after this there was no marked change. But a closer inspection revealed that the decrease becrease became less marked at distances of above 9 meters. With diameters of 26.8 and 19 cm the bends in the curve were seen at distances of 7 and 6 meters respectively, after which the decrease became small and tended to equal that seen for a diameter of 38 cm. If now we consider the state for a fixed size of the test-patch, with increase in visual distance there will result fallen in size of the visual angle, the latter showing in the beginning a rapid decrease up to a certain distance followed after this by a gradual decrease. Thus it was found that in the case of a 38 cm test-patch (diameter) of the previously described Experiment, the visual angle at a visual distance of 9 m was 2°24′, and differed from the visual angle for a visual distance of 10 m by 14′. Similarly for a diameter of 26.8 cm of the test-patch the visual angle at a distance of 7 m was 2°10′ ahd varied by 14′ from that for a distance of 8 m., while for a diameter of 19 cm, the value for 6 m was 1°48′ and varied by 16′ from the value for a visual distance of 7 m. From the above findings it may be considered that the reason for the fixity of f.f.f. at distances of more than a certain value, lies in (1) foveal vision occuring with decrease in visual angle (in this

case below 2°24′), and (2) the difference between it and the visual angle of the next visual distance (in this case below 16′) becomes negligible and produces practically no difference in the illuminated area of the retina. Hence when the test-patch is small the visual angle becomes rapidly small and the grade of decrease in size becomes also slight so that the break in the curve approaches the test-patch. However this break in the curve does not approach by 1/2 the distance even when the area of the patch becomes 1/2. In other words the greater the size of the test-patch the larger will be the pictrue seen from the break point of the curve. This fact provides a hint in the relationship of size of screen of a television set to visual distance. Next, even when the visual distance is altered, as may be seen from Fig. 4, f.f.f. is practically uninfluenced by distance if the visual angle is fixed in relation to the visual distance. This finding is extremely significant as f.f.f. will remain unchanged even if the visual distance is altered provided the visual angle is kept adapted to the distance. However, if the visual angle becomes altered, with the chang in visual distance there will result breaks in the curve as was seen in Fig. 2, 3, and 5. Such may be said to be due to the effects of the visual angle rather than to the visual distance. That the f.f.f. decreases slightly when the distance becomes great is believed to be due to the effects on the illuminating intensity of the test-patch brought about by the distance and of the size of the pupil.

On the effects of the illumination intensity of the test-patch. There have been extremely numerous reports regarding this problem. Oshima, Terazawa, Yamagishi, Hecht, Lythgoe and Tansley, Yonemura, Hashimoto, Kizaki, Fukano, etc., atated that the Ferry-Porter's law held good in their investigations or under a definite condition. In the present work too, it was demonstrated that f.f.f. rises if the illumination intensity of the test-patch is enhanced, and result similar to those by the above reported workers was obtained even when the visual angle was altered and when binocular vision was adopted. In addition a similar tendency was obtained whether test-patch was illuminated by the illumination of the room or not.

On the effects of the size of the pupil. Yonemura stated that there was increase of f.f.f. in the case of mydriasis induced by homatropin than in the case of the normal pupil, that f.f.f. gradually increases with artificial pupils of up to 5 mm, and that above 6 mm there was no change. Similar results were obtained in the present work. When the illumination intensity of the room was dark an artificial pupil of 5 mm, and when the intensity was 50 or 200 lx one of 3 mm showed f.f.f. corresponding with that of natural pupil. Such are believed to be due to the equalities in size between them. It was further found that the smaller the artificial pupil the lower was the f.f.f.. A characteristic feature was that in the case of artificial pupil there was a linear decrease in contrast with the unchangeability seen above a distance of 7 m in the case of natural pupil. This seems explanable when we consider that in the case of natural pupil there is seen dilatation with increase in distance, while in the case of artificial pupil there

will result decrease in the amount of light entering the eye.

Summary

Employing the Hagino-Suzumura's flicker apparatus, experiments were conducted to examine visual perception of flickering light under conditions where the visual angle, illumination intensity of the test-patch, illumination intensity of the room, visual distance and diameter of pupils were made to vary in a number of ways. The results obtained were as follows;

1. The greater the visual angle the greater was the f.f.f.. This phenomenen was seen even in cases where the visual angle was altered by changing the size of the test-patch or by changing the distance.
2. There is a difference in the f.f.f. between illumination of the examining room directed only at the area surrounding the flickering test-patch and that directed evenly throughout the entire room.
3. When the surface of the test-patch is illuminated by the weak illuminating light of the examining room the f.f.f. becomes higher than when not illuminated.
4. When the test-patch size is fixed and the visual distance is altered, the f.f.f. falls rapidly up to a certain distance, but when this distance is reached the degree of fall of f.f.f. becomes low, namely there is produced a definite bend. Even when the size of the test-patch is sltered the same tendency is noted, and the smaller the size of the patch the lower the f.f.f. becomes. And the smaller the size of the test-patch the nearer will the break of the curve approach the test-patch.
5. Beyond the break in the curve the influence of distance on the f.f.f. becomes weak and so also the value. Further there is seen difficulty of being influenced by illuminations of the room and other factors.
6. At a visual angle of 10° the influence of illumination intensity becomes greatest, and the smaller the size of the visual angle the lesser the influence becomes.
7. When the visual angle is adjusted to that suitable for a definite distance there is little influence of distance on the f.f.f..
8. The greater the illumination intensity of the flickering light the greater will be the rise of f.f.f..
9. The smaller the diameter of the pupil the lower the f.f.f. will become.

The above results cannot at once be applied to the problems of television viewing and others, as the present work was concerned mainly with the f.f.f. and no investigations were made on the perception of the picture. But it is believed that they have important significance.

The writer wishes to acknowledge his gratitude to Professor Hagino for valuable advice and guidance. He is also indebted to Dr. Suzumura for help and assistance.

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AN EXPERIMENTAL OBSERVATION UPON LYMPHATIC CHANNELS IN VITREOUS, RETINA, AND OPTIC NERVE

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Various studies have been made, since His' and Schwalbe's, upon the lymphatic channels of the retina and optic nerve, associated with those of the vitreous. These studies may be divided into perivascular and parenchymatous streams, but the thorough details are not known.

On the other hand, Ken Imachi, Jo Imachi, Ikui and others reported respectively upon the favorable results of the Leriche's operation, removal of carotid body, and superior cervical ganglionectomy for the disease of retinal degeneration, in improving vision, visual field, and hemeralopia, and they assumed that these favorable results were attributed to the elevation of blood pressure, dilatation of vessels, and the acceleration of the blood stream.

In this paper, however, the author attempts an experimental observation on the lymphstream, which is directly connected with cells, and wishes to make it clear how the stream alters, when the above-mentioned operations are performed.

Method

Using a white male rabbit of about 2kgs., the author injected 0.05 c.c. of pure Indian ink at the center of the vitreous body, and removed the eye-balls at interval (i. e., 1, 5, 10, 24 hours); fixed with liquid of Ciacio; embedded in celloidin, principally forming a series of horizontal slices; stained with hematoxylin-eosin, the van-Gieson stain, the Azan stain, then applied silver impregnation with the Bielschowsky-Maresh's. Proceeding with these procedures these slices were examined microscopically using these specimens as controls.

In the next place, using rabbits, on which the removal of perivascular sympathetic networks of both common carotid arteries (Leriche's operation) were previously performed and applied pure alcohol on the wall of the vessels; and on the other groups which the carotid body was previously exstirpated, the author injected 0.05 c.c. of Indian ink at 3-4 days after the operation. Another group of rabbits, which were left-side sympathectomized (superior cervical ganglionectomy) were also injected with 0.05 c.c. of Indian ink, when these rabbits showed paradoxical pupil dilation (reaction) by 0.1% of adrenalin

instillation at 7-10 days postoperatively.

From these rabbits, specimens were formed at 1, 5, 10, 24 hours respectively after injection as in the cases of the controls.

Result

Table 1 Distribution of free Indian ink particles

Hour after Injection	Case		At excavaton of optic disc	Lymphspace surrounding central artery: at the center of optic nerve	Lymphspace surrounding central artery: portion where it penetrates meninges	Surrounding of central vein	Septum of optic nerve	Intervaginal space
1 hour after injection	Control		−	−	−	−	−	−
	Leriche's operation		−	−	−	−	−	−
	Removal of carotid body		−	−	−	−	−	−
	Superior cervical ganglionectomy	operated side	−	−	±	−	−	−
		non-operated side	−	−	−	−	−	−
5 hours after injection	Control		−	±	+	−	−	±
	Leriche's operation		±	±	+	−	−	±
	Removal of carotid body		++	+	+++	+	+	±
	Superior cervical ganglionectomy	operated side	++	+	+++	+	+	±
		non-operated side	−	±	+	−	−	±
10 hours after injection	Control		+	+	++	−	+	±
	Leriche's operation		+	+	++	−	+	±
	Removal of carotid body		+++	+++	++++	+++	+++	++
	Superior cervical ganglionectomy	operated side	+++	+++	++++	+++	+++	++
		non-operated side	+	+	++	−	+	±
24 hours after injection	Control		+	+	++	−	+	±
	Leriche's operation		++	+++	+++	−	++	++
	Removal of carotid body		+++	+++	++++	+++	+++	++
	Superior cervical ganglionectomy	operated side	+++	+++	++++	+++	+++	++
		non-operated side	++	+++	+++	±	++	++

(−) Particles negative
(±) Particles slightly visible with strong magnification
(+) Particles clearly visible with strong magnification
(++) Particles slightly visible with weak magnification
(+++) Particles clearly visible with weak magnification
(++++) Particles smear pitch black

Table 1 shows the distribution of Indian ink particles in the retina and optic nerve at each hour.

Discussion

As an injecting dye into the vitreous body, the author employed Indian ink, the use of which in a minor quantity has been recommended by many since Seidel. The particles of this ink scarcely damage during a short time after injection, and, with its non-diffusive nature, it enables us to observe the lymphstream in the eye relatively in physiological stages. The quantity of 0.05 c.c. was decided on in view of the fact, that it appears to have the least influence upon the tension of the eye and, therefore, can be used most accurately.

In summary, the results are as follows:

One (1) hour after injection. Within the vitreous body, many carbon particles can be observed at the injected site extending backward to the optic disc, and along the vitreous membrane in front of the retina. These two flows of particles join together in front of the optic disc and are detained upon a thin membrane with one layer of endothelial cells in front of the optic disc (the limiting layer in front of the optic disc). Except for the operated side of the superior cervical ganglionectomy, however, carbon particles can not be seen either in the retina or in the optic nerve.

Five (5) hours after injection. In controls, carbon particles are detained on the limiting layer in front of the optic disc in increased quantity, while, although only in one case, quite a few free particles are observed in the excavation of the optic disc (one layer of endothelial cells surround the side of its vitreous and optic disc). Further, in the lymphspace surrounding the central artery, more carbon particles can be recognized as they reach closer to the intervaginal space of the opticus, although it is only visible with strong magnification. No particles are found in inter-septal lymphspace of the optic nerve and lymphspace surrounding the central vein. A minor deposit of particles can be observed in the intervaginal space of the optic nerve, close to the central artery penetrating the meninges.

To the above, the cases of the Leriche's operation and the cases of non-operated side of superior cervical ganglionectomy do not make much difference in the controls. In all cases of the Leriche's operation, partcles are (±) in the excavation of the optic disc, showing an opposit result to only one case in the controls.

In the cases of the removal of the carotid body and the operated side of superior ganglionectomy, a difference seems to be distinct, when compared with controls, as shown in Table 1. The deposit of carbon particles is positive (卄) in the excavation of the optic disc, and (+) (卅) in the lymphspace surrounding the central artery, the space being extended wider than in the cases of the controls. Quite a few particles in the septum of the optic nerve and the surrounding of the central vein can be seen. No particles in the parenchym of the retina and in the narrow space surrounding retinal

vessels are visible.

Ten (10) hours after injection. In controls, the deposit of carbon particles in the excavation of the optic disc is recognized (+), which is more than the deposit at 5 hours, increasing more as they come closer to the portion of meninges penetrated by the central artery where the deposit shows (++). In the septum of the optic nerve, a little deposit is found close to the central artery. In the surrounding of the central vein, and in the parenchym of the retina and optic nerve as well as in the narrow space surrounding the retinal vessels, particles are negative.

In the cases of the Leriche's operation and the non-operated side of superior ganglionectomy, the difference is more or less the same as with the controls.

In the cases of the removal of the carotid body, and the operated side of the superior ganglionectomy, a distinct difference can be recognized, deposit of carbon particles indicating (+++) in the excavation of the optic disc, but increases more toward the closer portion of meninges penetrated by the central artery. With the dilation of lymphspace, this portion looks like as if it was smeared pitch black by carbon particles. In the septum of the optic nerve, the deposit shows (+++), and particles are accumulated toward the subpial space. In the surrounding of the central vein, lymphspace shows extension with continuous deposit of (+++).

As a new fact in this case, a small amount of free particles can be recognized in the medullated nerve fiber layer of the optic nerve bundles in the proximity to the disc, and the same is true in the narrow space surrounding the retinal vessels. No particle, however, can be found in the deripheral retina and parenchym of the retina.

Twenty Four (24) hours after injection. In controls, particles deposit in the lymphspace surrounding the central artery in the amount equal to or a little more than the deposit of 10 hours. In septum a few more particles than those at 10 hours continually deposit (++) toward the subpial space. No particle are seen in the surrounding of the central vein, in the parenchym of the retina, and optic nerve.

Under 10 hours after injection, the presence of phagocytes is only small but increases at 24 hours, being less, however, when compared with free particles.

In the cases of the Leriche's operation and the non-operated side of superior ganglionectomy, a relatively marked difference with controls can be recognized at this hour, that is, the deposit is positive (++) (+++) in the excavation of the optic disc and in the lymphspace surrounding the central artery, but negligible in the surrounding of the central vein. In the septum, deposit continues (++), but no particles in the parenchym of the retina and optic nerve are visible. Phagocyte is present in equal amount to the controls or a little more.

In the cases of the removal of the carotid body and the operated side of the superior ganglionectomy, a marked difference with controls continues to exist as was seen at 10 hours, but the phagocyte is present in quite a large amount in the cases of superior ganglionectomy and most of the particles are being carried by this phagocyte.

Since the Leriche's operation was put into practice (to strip the sympathetic network of vascular walls of the artery), the technique of operation has attained a great improvement in various ways, but the operations adopted at present, as we call sympathectomy, are as follows:

1) Removal of the sympathetic network surrounding the carotid artery (application of alcohol, etc.)
2) Removal of the carotid body
3) Superior cervical ganglionectomy
4) Cervical and thoracical ganglionectomy or stellectomy.

Based on the results of the above mentioned operations, a number of clinical findings have been reported. For example,following is the Magitot's finding (1934).

In treating the diseases of degeneration in the retina and optic nerve, he stripped the vascular walls of the internal carotid artery, oppressed the portion of the carotid body, and observed its process. Soon after the operation, the decrease of blood pressur occured and continued for 24-36 hours. After that, the pressure began to take an opposit trend and increased in a higher rate than the preoperative condition for the period of 2-4 days, and decreased again in a slow wave until it came down to the preoperative value. In this case, improvement of vision, visual field, etc. was noticable. He assumed, therefore, that these improvements were caused by the elevation of blood pressure, and, provided, that the nerve tissues under the deficiency of nutrition were not completely damaged, their functions would be recovered by the provoked permeability of the capillary and by reopening of the closed capillary as well as the dilation of retinal vessels. Further, he added that, for retinitis pigmentosa, these would accelerate the blood stream in the thyroid gland, hypophysis, and mesencephalon, and, in addition, would change the balance of inner secretion.

Abadie, Lauber, Ken Imachi, Blobner, and others performed the Leriche's operation for retinitis pigmentosa; Nizètić, Jo Imachi, Inoue and others, removal of carotid body; Royle, Kerr, Meigham, Campbell, Walsh and Sloan, Ikui and others, superior cervical ganglionectomy. All of them attributed the favorable results of these operations to the dilatation of vessel and the acceleration of the blood stream.

The author attempts, however, to observe these favorable results in relation to the alteration of the lymphstream.

The lymphstream which flows in from the vitreous body backwards, runs mainly through the lymphspace surrounding central vessels and comes out into the orbit. This lymphspace has both wide and narrow portions and, therefore, it may be assumed, that the rate of the lymphstream penetrating into the connective tissues, which compose the lymphspace, varies in portion according to the type and density of the tissues.

Observing the process of the controls, it is found that the inside of the excavation of the optic disc is wider, when compared with the others, and the connective tissues

being slack, resistance of the lymphstream is very small. The deposit of Indian ink particles are also few. The lymphspace surrounding the central artery in the parenchym of the optic nerve becomes rather narrower, tissues thicker, and the resistance of the lymphstream increases. The deposit of particles is also found to increase. In the portion of meninges penetrated by central vessels, the space is very narrow, and with the dense connective tissues surrounding the artery, the resistance here is thought to be the strongest. The deposit of particles is also at its most. Consequently, if the lymphstream of Indian ink particles, which flow in over the limiting membrane before the optic disc, should be accelerated at a rate sufficient but not to exceed the resistance in the portion of meninges, particles would be piled up in the portion of meninges, extending toward the side of the vitreous body as a trace of stream.

It is not obvious how these streams surrounding the central vessel are produced, but, locally, the analog may be found in Virchow-Robin's space of brain. If the stream is thought to be produced by pulsation of the vessels, as Belloni, Rijssel and others assert, it may be assumed that the tension of the walls of the vessels will be decreased by isolating the central vessels from the sympathetic impulse, and the change of pulsation type will accelerate the lymphstream.

In the cases of the Leriche's operation and the non-operated side of the superior cervical ganglionectomy, the flow of the lymphstream is a little more accelerated than in the cases of the controls, but the accumulation of such a minor difference with the controls may be considered to make a relatively marked difference at 24 hours after injection.

In the cases of removal of the carotid body and the operated side of the superior cervical ganglionectomy, the lymphstreams are amazingly more accelerated than the controls. Therefore, carbon particles have shown a distinct increase all through the 5-24 hours. In this case the deposit of a particle can be recognized in the lymphspace surrounding the central vein and among the nerve fibers of the medullated nerve fiber layer of the retina. Such deposits are not noticeable in the controls and it may be assumed, that this accounts for the dilation of all lymphspaces and the existence of much liquid in the tissues, diffusing from the capillary.

Evans reports that there is a space surrounding the smaller vessels of the retina which is similar to Virchow-Robin's space, and this space is connected with the spaces surrounding nerve cells and nerve fibers. If the space surrounding smaller vessels of the retina should be considered the same with that of the central vessels, the stream of this space would also be accelerated accordingly, giving influence to the space surrounding nerve cells and nerve fibers.

The author's conclusion is that the acceleration of the lymphstream together with the extension of lymphspace have revealed to be effective for degenerative diseases of the retina by isolating the central vessels from the sympathetic impulse.

Summary

At the center of the vitreous body of white male rabbits of about 2 kgs., the author injected 0.05 c.c. of pure Indian ink solution, removed the eye-balls after 1-24 hours in order to investigate the distribution of Indian ink particles microscopically in the series of slices.

On the other hand, the author performed the Leriche's operation, removal of carotid body, and superior cervical ganglionectomy, and investigated microscopically in comparison with the controls.

1. In the cases of Leriche's operation and the non-operated side of the superior cervical ganglionectomy, the lymphstream shows acceleration than in the cases of the controls.

2. In the cases of removal of the carotid body and the operated side of the superior cervical ganglionectomy, the lymphstream is accelerated much more remarkably when compared with the controls, and shows a dilation in all lymphspaces.

3. From the above, it is clear that the so called sympathectomy causes the acceleration of the lymphstream and dilation of lymphspace, and reveals to be effective on the retinal degenerative diseases.

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THE SIGNIFICANCE OF THE OCULAR CHANGES BY THE SHOCK STIMULI

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In the preceding papers,[1,2,3,4,5], studies were made of the effects of the convulsive (electro-, cardiazol and insuline) shocks on the eye with the following results:

The main ocular change following the single stimulation was the fluctuation of the ocular tension, such as a drop of tention in the shock phase and a tendency of rise of tension several hours after the shock phase. In the course of the repeated daily shock stimuli, the eyes showed uniform changes, namely, distinct and continuous drop of ocular tension, superficial corneal opacity, retinal detachment, appearance of unique gaseous and oily substances and bleeding in the choroid, regardless of the kind of stimuli.

In this paper, the interrelationship between ocular changes and their relationship

to the general conditions, especially vital reactions induced by shock stimuli will be discussed.

1. The relationship between the change of ocular tension and the vital reactions by shock stimuli.

In the so-called shock state, it is usual to observe mental confusion, the decrease of temperature, disturbance of the respiratory and circulatory system and changes of blood components, always showing the hignest impediment of autonomic nervous functions.

As to the state of the autonomic nervous system under a shock phase, Loman, Rinkel and Myerson[6] (metrazol shock), Domm, Gellhorn[7] and Kuromaru[8] (insuline shock, electro-shock) proved the decrease of CO_2 in the arterial blood during the shock period which was explained with the excitement of the sympathetic nerve center. Sugita[9] reported the leucocyte picture during the period of electric and cardiazol shock, which showed the augmentation of the sympathetic function.

On the other hand, as to the behavior of the hypophyseo-adrenocortical system, Early (1951), on thebasis of the eosinophilic count, uric acid/creatinine ratio and the urinary excretion of 17-KS after electro-shock, estimated the potency of electro-shock as stronger than two 50mg ACTH tablets, and Novelli (1950) proved hypertrophy of the adrenal cortex and accumulation of eosinophilic and colloid-like material in this organ. Paschkis et al. (1950) certified the increase of corticoids in the adrenal vein and peripheral blood. Adreno-cortical hypertrophy was proved in insuline shock (Abert, 1950) and metrazol shock (Pekkarinen, 1951). Hoagland,[10] Graham,[11] Raskin,[12] Kuromaru and Sugiyama[13] took the activation of the hypophyseo-adrenocortical system into consideration on the basis of the marked decrease of eosinophil cells and lymphocytes in blood following the electric and insuline shock.

These experimental results all demonstrate, that shock stimuli work on the organism as a powerful stressor, and, in other words, cause vital reactions mostly attributable to the excitement of the sympathetic nerve center and the activity of the hypophyseo-adrenocortical system.

On the other hand, marked changes in the ocular tension were observed synchronously with the vital reaction following shock stimuli, i. e., drop of ocular tension was observed in the excitement state of the sympathetic nerve center. A tendency of increase of marked fluctuation of the ocular tension several hours after the shock phase corresponds to the active stage in the hypophyseo-adrenocortical system, as shown in the decrease of eosinophil cells and lymphocytes in the blood and the increase of blood sugar.

These findings are very suggestive as to the relationship between stress and ocular tension. Ikeda[14] has shown his interest especially in this problem. According to him, glaucoma is often induced by stressors such as cold, emotional excitement, mental strain, eye-operations, etc. Suggesting that glaucoma may be induced as a vital reaction

(alarm reaction) in stress. On the basis of the author, it may be presumed as follows: as vital reaction in stress is non-specific, the mode of variation of ocular tension following stress is similar to the changes after shock as shown by this experiment.

Now, in cases of a single stimulus as well as repeated stimuli, ocular tension mostly showed decrement.

This phenomenon is not merely limited to shock stimulus, but is also seen in cases of the other stressors. For example, pain stimuli, alarm stimuli, repeated intravenous injection of adrenaline are known to induce a drop of ocular tension. Then how are we explain the fact, that a glaucoma attack is often caused by a stressor? As described previously, ocular tension shows mostly descent by a stressor. While such changes were observed relatively soon after the stimuli, the fact, that a rise or fluctuation of ocular tension seems to be synchronous with the defence reaction of the organism, i. e. the promotion of hypophyseo-adrenocortical system activity, is considered to give a suggestion of the relationship between the defensive mechanism of the organism and ocular tension, as well as incidence of glaucoma attack in stress.

2. The relationship between variations of ocular tension, corneal opacity and choroidal changes.

As the corneal opacity and the drop of ocular tension are consistently observed synchronously, the existence of a direct relationship between them might be considered. For example, it might be assumed, that the drop of ocular tension induced a superficial corneal opacity. But it is more adequate to consider that there exists no direct relationship between them, but a common agent, for instance, abnormality of salt and water metabolism, or a decrease of aqueous circulation and production.

Furthermore, the relationship between choroidal changes and ocular tension can not be ignored, because the hemorrhage, the unique substances in the choroid and the retinal detachment are consistently observed at the period of the marked drop of ocular tension.

In order to detect the relationship between the drop of ocular tension and the appearance of choroidal changes, the following experiment was done. A part of the vitreous fluid of the normal rabbit's eye was drawn and the fellow eye was left untreated as a control. When shock stimuli were repeatedly given to the animal, the choroidal changes appeared in a very early stage and markedly in the pre-treated eye.

This finding shows clearly that there is a close relationship between the drop of ocular tension and the choroidal changes.

3. The character and the clinical significance of ocular signs following repeated shock stimuli.

1) The character of the ocular signs.

As mentioned above the changes of the cornea, the choroid and the ocular tension show consistently similar features following repeated shock stimuli regardless of the mode of stimulation.

Such ocular changes are known to appear by not only shock stimuli, but also by repeated systemic stressors of any kinds. For instance, corneal changes are observed following repeated intravenous injection of adrenaline, acetylcholine and histamine, moxibustion, accumulation of heat and electric irritation of the ears and legs of the rabbits. The choroidal changes are also observed following the intravenous injection of adrenaline and acetylcholine, moxibustion and accumulation of heat. These ocular changes are named "nonspecific ocular reactions"[15] and their non-specific nature is thought to depend on the vital reaction.

In these experiments of repeated shock stimuli ocular changes are found closely related to the systemic conditions. This relationship is clearly shown by the comparative examination of the ocular changes, chloride content in the blood and distribution of lipid granules in the adrenalcortex as shown in Table 1; the relation between the lipid distribution in the adrenocortex and the state of G-A-S is obvious on the basis of the experiments of Ikeda et al.[16] and Selye's G-A-S.

Corneal opacity is observed mostly at the stage of alarm reaction and the stage of exhaustion. The appearance of unique substances or hemorrhage in the choroid, and detachment of the retina were observed at the stage of resistance especially at the latter part of it.

The ocular tension showed mostly a tendency of drop through the whole period following repeated shock stimuli.

Thus the appearance of ocular changes is closely related to general stress caused by repeated shock stimuli. It is especially interesting, that choroidal changes appear immediately after shock stimuli under the most susceptive condition which is called "non-specific sensitization"[17], regardless of the sort of stimuli employed.

It had been stated, that factors which cause non-specific reaction of the choroid exist in the general cocdition of the rabbit, and that a factor which directly causes the reaction is the sympathin liberated from the adrenal cortex by shock stimuli, Of the shock stimuli in the present experiment too, just the same can be considered.

2) The clinical significance of ocular signs.

From the above observation, it becomes clear that ocular signs following shock stimuli are counted in the "non-specific ocular reaction". Such reaction is full of clinical suggestions: for instance, the corneal opacity has many resemblances to the superficial corneal opacities of man, while the choroidal changes seem to give a clue to make clear the developmental mechanism of changes of the fundus (opacity, edema, hemorrhage etc.) in the man's retinopathies, because retinal detachment or edematous turbidity observed in the process of non-specific choroidal reaction resembles, to a great degree, the serous central chorioretinitis (Masuda) of man. Thus it is considered possible that the both conditions of rabbit and man have a same origin.

a) The eliciting and developing mechanism of central chorioretinitis. From our clinical statistics of 90 cases of central serous chorioretinitis it became clear that the

Table 1

Rabbits	Sort and Frequency of Shock Stimulus	Distributrion of Lipid in Adrenal Cortex									
		Neilblue Staining Metachromasia					Sudan III Staining				
		G	Fa	Fb	Fc	R	G	Fa	Fb	Fc	R
10	E S, 38	−	+	−	+	−	±	±	±	+	+
12	E S, 37	±	±	++	+	+	++	++	++	+	+
13	C S, 14	+	+	+	+	+	+	++	+	+	+
14	E S, 8 C S, 8	±	++	++	+	−	+	++	+	+	+
16	I S, 14	−	−	+	±	+	±	±	+	±	+
20	E S, 24	−	+	++	++	+	+	++	++	++	+
21	I S, 7 E S, 15	−	+	+	++	+	+	+	+	+	+
22	E S, 6 NaCl 2gm./day Administer	±	++	+	+	+	±	±	±	±	±
31	C S, 15 E S, 16	−	−	±	++	+	+	±	±	±	++
32	E S, 18	±	+	++	+	+	++	++	++	++	++
33	E S, 29 C S, 10	±	+	+	++	+	+	+	+	++	+
34	C S, 16	±	+	++	++	+	+	++	++	++	+
40	E S, 14 Fractur of Femur	−	±	−	+	++	±	±	±	+	+
43	E S, 15	±	+	++	+	±	+	++	++	++	++
44	E S, 26	−	−	+	++	+	+	+	+	++	++
46	C S, 20	±	+	+	+	++	+	+	+	+	++
47	E S, 26	−	−	+	+	+	±	±	±	+	+
50	E S, 14	−	−	+	+	++	±	+	±	+	+
51	C S, 9 Fractur of Femur	−	±	+	+	++	+	±	±	+	+
52	Control	±	+	++	+	+	++	++	++	++	++
53	Control	+	+	++	++	+	++	++	+	++	++
54	Confrol	±	+	++	+	+	++	++	+	+	++

G: Zona glomerulosa, F (a, b, c,): Zona fasciculata (outer, median, inner),
R: Zona reticularis. ES: Electro-shock, CS: Cardiazol shock, IS: Insulin shock.

eliciting and developing mechanism is closely related to the systemic stress such as cold, mental insults and various diseases.

b) The clinical picture of central serous chorioretinitis.

While the changes of the disease are localized mostly to the macular region, the

Geneal Condition and Days till Death	Stage of GAS	Ocular Changes		
		Corneal Opacity	Choroidal Changes	Ocular Tension
Gradually Emaciation Death 39	S E	###	Hyperemia, Hemorrhage	
Good, Slaughter 37	S R	+	Hyperemia, Hemorrhage Apperrance of Unique Substance	
Good, Slaughter 14	S R	—	Hyperemia, Appearance of Unique Substance	Drop
Good, Slaughter 13	S A→S R		Amotio retinae, Hemorrhage, Appearance of Unique Substance	Drop
Gradually Emaciation Death 15	S A→S E	##		
Good, Slaughter 24	S R	+	Hemorrhage, Appearance of Unique Substamce	
Good, Slaughter 22	S R→S E	±	Hemorrhage, Appearance of Unique Substance	
Good, Sudden Death (Asphxia) 6	S A→S R	##	Hyperemia	
Gradually Emaciation Slauguter 33	S R→S E	##	Hyperemia, Appearance of Unique Substance	
Good, Slaughter 18	S R	—	Hyperemia	
Emaciation Slaughter 40	S R→S E	##	Hemorrhage, Appearance of Unique Substance	
Good, Slaughter 16	S R	—	Hyperemia, Appearance of Unique Substance	
Gradually Emaciation Death 15	S A→S E		Anemic	Drop
Good, Slaughter 15	S R		Hyperemia, Appearance of Unique Substance	Drop
Good, Slaughter 26	S R→S E		Hyperemia, Appearance of Unique Substance	Drop
Good, Slaughter 20	S R		Hyperemia, Hemorrhage, Appearance of Unique Substance	Drop
Gradually Emaciation Death 27	S E	##	Anemic	Drop
Rapid Emaciation Death 7	S A→S E	##	Anemic	Drop
Rapid Emaciation Slaughter 10	S A→S E	###	Anemic	Drop
Good				
Good				
Good				

SA: Stage of Alarm Reaction, SR: Stage of Resistance.
SE: Stage of exhaustion,

non-specific choroidal reaction of rabbits is mostly localized to the posterior pole, and has a tendency to spread out horizontally along the horizontal meridian of the eyeball. This is based on the difference between the vascular distribution of the choroid of man and that of rabbit. The sites of the change coincide, in that both are at the

branching point of the arteria choroidea, after entering the choroid through the sclera. In non-specific choroidal reaction, edema or detachment is frequently observed in both of the eyes simultaneously, while the central serous chorioretinitis is usually observed in one eye. However, even in the former, when given a weak stimulus, only one eye can be affected.

While in the former bleeding with retinal edema or detachment is frequently observed, this is of rear incidence in the latter. However this may be due to the fact that the choroidal hemorrhage in man's fundus is difficult to detect. Because even in cases of the choroidal reaction of rabbits, hemorrhage is not observed but only edema is observed following weak stimulus, the difference in the reaction of rabbits and the disease of man is considered to depend on nothing else than the intensity of the given stressors. Thus it may be said that between non-specific choroidal reaction and central serous chorioretinitis there is no fundemental difference. As in the case of rabbit's choroidal reaction following shock stimuli, the stimulation of the sympathetic nerve center or liberation of sympathin in stress caused by mental insults, cold, diseases, etc. is considered to constitute the main agent in the incidence of central serous chorioretinitis of man.

Summary

It is concluded that various ocular changes following shock stimuli may be the expression of vital defence reaction which should be illustrated by the systemic autonomic nerve modulation and the manifestation of the hypophyseo-adrenocortical system action, which offers an important implication in order to make clear developmental mechanism of glancoma, superficial keratitis and central serous chorioretinitis etc. in man.

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ON APPEARANCE-RATE OF THE RING OF A RAINBOW TINTS IN GLAUCOMATOUS PATIENTS

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It has been known for long, that a ring of rainbow tints appears in glaucomatous patients and there might be nothing new to say. But as I have recently had an opportunity to bring my work to completion as a part of glaucoma-research in this classroom, I would like to make it public.

Materials

As materials of research I picked up in and out-patients of the Eye Clinic of Nippon Medical College for the past five years since 1952 to 1956, whose protocols were clearly described. To be definite, they were 61 congestive glaucomatous patients (94 eyes), 38 simple glaucomatous patients (63 eyes) and 9 glaucoma-suspicious patients (16 eyes); in total 108 patients (173 eyes).

Results

The first tabular statement shows the appearance rate of a ring of rainbow tints according to different types of glaucoma. In congestive glaucoma, the ring was checked to have appeared in the past in such many cases as 78.7 pent. In simple glaucoma, however, the ring was recognized in the past at the rate of 27.0 per cent: a very small number as compared with congestive glaucoma. In patients who were diagnosed as glaucoma-suspicious, the appearance rate in the past was 37.5 per cent.

Table 1 The appearance rate of a ring of rainbow tints according to types of glaucoma

Type of disease	Total	Ring positive eye		per cent
Congestive glaucoma	94	Bygones	74	78.7
		At the first exam.	15	16.0
Simple glaucoma	63	Bygones	17	27.0
		At the first exam.	2	3.2
Glucoma suspicious	16	Bygones	6	37.5
		At the first exam.	0	0

The second table shows a relationship between a ring of rainbow tints and opacity of the transparent materials in cases, where the ring was perceptible at the first medical examination. It tells us that in almost all cases in which the ring was perceptible, dullness of cornea was observed. It is learnt that there is a close relationship between the two.

The third table indicates the size and the colortone of the ring of rainbow tints,

measured from a meters distance, using a miniature bulb of 6 volt and a campimeter. The size was irregular with each individual. It was between one degree (inwards) and ten degrees (outwards) and drew a circle around the bulb. The color tone also was unsettled; some were observed in an order of red (inwards) to blue (outwards) and some others were just in a reversed order of blue to red. And there was a case with which only a single color was observed.

Table 2 The relationship between the ring and the transparent materials

Type of disease	Ring positive	Dullness of cornea	Opacity of the lens	Opacity of the vitreous body
Cong. glaucoma	15	14	3	0
Simple glaucoma	2	2	0	0

Table 3 Size and color tone of the ring

Type of disease	Case	Age	Sex	Ring (from the inside)
Congestive glaucoma	K. F.	29	M	R. red-yellow L. red-yellow
	T. K.	48	F	L. red-yellow-blue
	H. O.	50	F	L. red-yellow-green 6° ——— 8°
	R. N.	52	M	R. red-blue 2.5°-3.5°-4.5° L. blue-red-blue-red 2.5°-3.5°-4.5°-5.5°-6.5°
	M. T.	63	F	R. red-green
	K. K.	66	F	R. blue-yellow-red 1°——2°——3°——4°
	K. K.	67	M	L. red-yellow-green 3° ——— 5°
	T. T.	79	F	L. blue 5°——10°
	K. T.	54	F	R. blue-yellow-red 1°——2°——3°——4°
Simple glaucoma	T. U.	52	M	R. yellow-blue-yellow-blue L. yellow-blue-yellow-blue
	A. K.	54	M	R. yellow-blue
Glau. suspicious	S. T.	55	F	R. blue-yellow-red-violet

M: male R: right
F: female L: left

The fourth table is a result of an inducing examination of the ring, raising intra ocular tension by pressing the bifurcated region of A. carotis communis with 30 mmHg for 10 minutes. In 3 eyes out of 10 of congestive glaucoma the ring was clearly observed to appear after they were pressed which was not discernible before the test. However, in 7 eyes of simple glaucoma no such a case was observed.

Table 4 The results of an inducing exam. of the ring of rainbow tints

Type of disease	case	Age	Sex	Intra ocular tension		The ring		Remarks
				Before v. p. t.	After v. p. t.	Before v. p. t.	After v. p. t.	
Congestive glaucoma	K. F.	29	M	R. 26 L. 26	26 32	— —	— —	
	T. M.	41	F	R. 30 L. 30	36 30	— —	+ —	Elliot's operation
	T. K.	48	F	L. 50	66	—	+	
	R. N.	52	M	R. 70 L. 65	80 75	+ +	+ +	
	K. Y.	60	M	R. 36 L. 56	49 66	— —	— +	
	M. T.	63	F	R. 48	66	—	—	
	K. Y.	67	F	R. 26	22	—	—	Iridectomy
	S. M.	80	F	L. 56	68	—	—	
Simple glaucoma	K. Y.	23	M	R. 48 L. 40	56 48	— —	— —	
	S. H.	28	M	R. 22 L. 33	26 26	— —	— —	
	Y. F.	28	M	R. 19 L. 22	25 25	— —	— —	
	H. K.	54	M	R. 26	35	—	—	
	M. I.	57	M	L. 30	40	—	—	

v. p. t. : venous pressure test
M: male F: female

Synthesis and Discussion

It has been known for long, that the ring of rainbow tints appears in glaucomatous eyes. But opinion is divided on cause and mechanism of its appearance. Koeppe (1920) asserts that it appears by refractive function of light being caused by opacity of the vitreous body. Druault (1923) states that opacity of the lens is also the cause of the appearance. But it is generally supported, that it appears by refraction of light because of dullness of corneal epithelia, chiefly of oedema. Accordingly, the same phenomenon happens to be observed by refraction of light when secreta of conjunctivitis cover the cornea as a sort of membrane, but it usually vanishes with irrigation. Also, a report tells us that the same is observed in a special type of cataract. Or, in the normal lens, it is sometimes observed when mydriasis is present. So, the ring of rainbow tints is not a symptom specific to glaucoma, but, at the same time, it is out of the question, that it appears at the highest rate with glaucoma. Especially in congestive glaucoma, as stated above, its apperance rate is as high as 78.7 per cent. Even with simple glaucoma, the ring becomes to be noticed in a great many cases when it developes to transitional form. In congestive glaucoma, some are observed at their prodromal stage and some others at their active stage. But the point is that it

is probable to appear when the transparent materials of the eyeball becomes dull. So, a research has been made on relationship between the ring and dullness of the transparent materials. It resulted that in the corneas of eyes, in which the ring was perceptible, dullness was positively observed in most cases. Here, the hitherto supported theory, that the ring of rainbow tints does appear by refraction of light being caused of corneal oedema was justly confirmed, The size of the ring was irregular with each individual, when measured from one meter distance using a miniature bulb of 6 volt.

As for the color order of the ring, some one says, red to violet (from the inside towards the outside) and others say blue to red. But through the investigation it is learnt that the color order is not quite settled. That is, in some cases it was observed in an order of red to blue and in some others of blue to red. Also, we had such cases, in which the right eye was in an order of red to blue and in the left one of the same person blue to red. Or, there was a case in which only a single color was observed.

Next, we made a test by pressing the bifurcated region of A. carotis communis with 30 mmHg for 10 minutes, in order to see if the ring of rainbow tints should appear. In 3 eyes out of 10 of congestive glaucoma the ring was noticed to appear after pressed, which was by no means discernible before the test. It is thus considered, therefore, that the ring did appear because venous pressure test raised intraocular tension, which caused oedema or dullness of the cornea.

Conclusion

1. A ring of rainbow tints was observed in 74 eyes out of 94 congestive glaucomatous eyes (78.7%), and in 17 eyes out of 63 simple glaucomatous eyes (27.0%). The ring was also observed in 6 eyes out of 16 glaucoma-suspicionus eyes (37.5%).

2. The ring in glaucomatous eyes has a close relationship with corneal opacity.

3. The color order of the ring in glaucomatous eyes is arranged according to the spectrum order of red to blue or blue to red. But there is also a ring comosed of a single color.

The size of the ring covers, when measured from a meters distance using a miniature bulb of 6 vol, the region between one degree and ten degrees and drew a circle around the bulb.

4. The ring was induced in a congestive glaucoma by pressing the bifurcated region of A. carotis communis with 30 mm.Hg for 10 minutes.

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STUDIES ON THE AUTONOMIC EYE PRESSURE ADJUSTMENT FUNCTION OF THE NORMAL EYE

Part II. Studies on the Efferent and Afferent Tracts of Autonomic Eye Pressure Adjustment Reflex and the Effector Organs.

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I. Studies on the efferent and afferent pathways of autonomic eye pressure adjustment reflex

It has been demonstrated that the diencephalon is the site at which the eye pressure is regulated. However, the efferent tracts actually carrying the impulses of the adjustment center of the eye pressure to the eyeball and the afferent tracts transmitting the variations of intraocular pressure to the center regulating eye pressure still remain to be solved. With a view to clarify these, the author conducted the present experiments.

A. Studies on the efferent pathways of eye pressure reflex

As is well known, many autonomic functions such as blood pressure, pupillary activity, and respiratory rate, are regulated by the autonomic nervous system. This being so, for the clarification of the mechanism of the autonomic eye pressure reflex, the autonomic nervous system seems to be the first point of approach.

Experiments and Results

1) The relation between eye pressure and the sympathetic nerve[10].

Among the literatures concerning this problem, there are reports by such investigators as Henderson and Starling[1], Adamück[2], Wessely[3], Stock[4], Yada[5], Colle and Duke-Elder[6], Jaffé[7], Davson and Matchett[8], Greaves and Perkins[9], and others, but their results do not necessarily concur with each other. Therefore, with an intention to re-examine this point, observations were made on the changes in the intraocular and the systemic blood pressures and on the behavioral patterns of pupils and exophthalmos by stimulating the cervical sympathetic nerve electrically under various conditions. All the experiments were carried out on normal adult rabbits. In the following the results are described divided into 4 sections.

Relationship between stimulation in the sympathetic nerve and the eye pressure. The results on the 12 rabbits differ somewhat according to the changed intensity of stimuli. In cases of weak stimulation, the eye and the systemic blood pressures decreased as a rule, but in the majority of them mydriasis or exophthalmus could not be found. On the other hand, in the cases of strong stimulation the eye pressure either decreased or

increased although systemic blood pressure fell in all cases. In the cases showing an increase in both blood pressure and eye pressure, marked mydriasis and exophthalmos were generally recognized.

The relationship between the stimulation of sympathetic nerve and the intraocular pressure on the unstimulated side. In order to confirm whether or not the changes of the eye pressure occurring at the time of the stimulation of the cervical sympathetic nerve are effected by the changes of the systemic blood pressure, the changes of the eye pressure on the unstimulated side have been investigated at the time of unilateral stimulation of the cervical sympathetic nerve. In these experiments, the intraocular pressure of the eye on the unstimulated side showed little or nn change, and even in the cases showing a slight decrease, the decreasing grade was far less comparing to those on the stimulated side. Therefore, the fall of the eye pressure at the time of the stimulation of the cervical sympathetic nerve seems to be not effected solely by the changes of systemic blood pressure.

The effects of the resection of the cervical sympathetic nerve on the eye pressure. The resection of the cervical sympathetic nerve, including superior cervical ganglion, caused the rise in both the intraocular and the systemic blood pressures.

Influences of the resection of the cervical sympathetic nerve on the rise of the eye pressure caused by the compression of the jugular vein. By a mechanical compression of the jugular vein, the eye pressure usually tends to rise; and the rate of the rise in the case of the rabbits with prior resection of the cervical sympathetic nerve is more marked than that of the untreated ones. This fact seems to suggest that the cervical sympathetic nerve possesses the functions inhibiting a abnormal rise of the eye pressure.

Summarizing these results, it will be said that the excitation of the cervical sympathetic nerve seems to serve essentially in the lowering of the eye pressure by transmitting the impulses inhibiting abnomal rise of the eye pressure. However, when the stimulus is so intense as to cause the contraction of intraorbital smooth muscles, the eye pressure seems to rise by being effected by the muscular contraction itself.

2) The relationship between the oculomotor nerve and the eye pressure[11].

Extensive studies on this subject have been undertaken by numerous investigators such as Imachi[12][13], Saito[14], Schmerl and Steinberg[15], Greaves and Perkins[16], Agarwal[17], and others, but their results do not necessarily coincide with each other. In order to clarify the role of the oculomotor nerve in the regulation of eye pressure the author has conducted the following experiment.

By anesthetizing rabbits with Urethan, the skull was opened to expose the oculomotor nerve which was electrically stimulated. Now, the changes in the intraocular and the systemic blood pressures, the behavioral patterns of pupils, and the width of lid fissures occurring at the time of stimulation were recorded simultaneously. Marked rise of the eye pressure has been observed in all cases; namely, the eye pressure rises rapidly

simultaneous with stimulation of the oculomotor, whereas it falls quite swiftly immediately after the cessation of stimulation. Miosis and the widening of lid fiissures have been seen in all cases. The systemic blood pressure is kept in the normal range. As for the eye on the unstimulated side, hardly no change of pressure can be recognized. From the above observations, as the rapid rise of the eye pressure seen immediately after the stimulation seems to be in a large measure due to the contraction of ocular muscles, a similar experiment was conducted with a rabbit whose extrinsic ocular muscles had been cut and subjected to scrutinous akinesy.

In this experiment, miosis was found in every case; however, the widening of lid fissures could not be observed except in one case. The rise of the eye pressure in this experiment were similar to those of the preceding experiment, though the amplitude of the rise was less. From these results, it seems that the excitation of the oculomotor is responsible for the rise of the eye pressure, and that its mechanism is mainly dependent on the contraction of ocular muscles, though other factors can not be entirely ignored.

3) Influences of ganglion blocking agents on the changes of eye pressure caused by compression of the eyeball[11].

In the previous papers, the author has demonstrated that the mechanical compression of the eyeball brought about a sudden elevation of the eye pressure, but after a while the eye pressure began to descend, slowly reaching the original level after 5-10 minutes, on the average of 6.6 minutes. The author, however, has found that in the rabbits administered venously with ganglion blocking agents such as Teabrom (tetraethylammonium bromide) or Imidalin (benzylimidazolin) prior to the compression of the eyeball, the consequential decrease did not occur.

4) The influences of ganglion blockage upon consensual ophthalmotonic reaction[11].

The author has mentioned in his previous report that when the intraocular pressure is artificially elevated unilaterally by mechanical compression, the pressure of the unstimulated eye in contrast falls. The author in this experiment has been able to prove, that no such consensual ophthalmotonic reaction appears, if the superior cervical ganglion on the side opposite to the side to be stimulated, is coated with 1% Nicotin solution or the cervical sympathetic nerve including its superior cervical ganglion is removed prior to the stimulation. On the contrary, in the cases resected of their cervical sympathetic nerve on the same side of the eye to be stimulated, this reaction remained unaffected.

5) The influences of ganglion blocking agents on the changes of eye pressure caused by the stimulation of the diencephalon[11].

The author has introduced ganglion blocking agents, namely, 20 mg. of 2-benzylimidazolin or 100 mg. of tetraethylammonium bromide, intravenously into the adult rabbits and observed how the intraocular and the systemic blood pressures, the behavioral pattern of the pupils, and the width of the lid fissures might be affected at the time of stimulation of the diencephalon.

As the results, the changes of the intraocular and the systemic blood pressures which occurred in the stimulation of diencephalon before the injection, either disappeared or diminished after the injection. Form this fact, it may be assumed that the impulse from the interbrain seems to be transmitted by way of the autonomic nerve to the eyeball.

Conclusion

From these experimental findings, it may be concluded, that the autonomic nerve an important role in the regulation of the eye pressure, and that the impulses in the eye pressure adjustment center seem to be transmitted by way of efferent pathways of the autonomic nervous system; namely, the sympathetic nerve works the impulse to lower the eye pressure, while the parasympathetic nerve exercises the impulse to raise the eye pressure.

B. Studies on the afferent pathways of autonomic eye pressure reflex[15].

Henderson and Starling[1] point out that the Vth cranial nerve participates to a great degree in the regulation of eye pressure. More recently, many investigators such as Moreu[18], Courtis and Nunez[19], Perkins[20], and others report that the trigeminal nerve plays an important role in the development of glaucoma. Lately, Perkins[20] proves that a mechanical stimulation of the trigeminal nerve causes a marked increase of the eye pressure by dilating uveal vessels as by raising the temperature of the ciliary body.

The author has investigated from various angles whether or not the Vth cranial nerve might be involved in the regulation of eye pressure.

Experiment and Results.

By making an incision of the skin of a rabbit the point half way between the ear-hole and the external ocular angle, and by advancing deeper while parting the subcutaneous muscles right and left, the condyloid process of the submaxillary bone was uncovered. By removing a part of this bone and advancing still deeper while separating the muscles, the tympanum of the temporal bone was exposed. The branch of the ophthalmic nerve was easily found in the anterior part of the tympanum. Then, after cutting this nerve, its proximal or its distal end was electrically stimulated and the reactions of the intraocular and the systemic blood pressures, changes of pupils, and the responses of nictitating membrane were simultaneously recorded and traced continuously. Observations were carried on with rabbits with or without treatment by Curare.

1) Relationship between the stimulation in the trigeminal nerve and the eye pressure.

Stimulation at the proximal end of the nerve. The electric stimulation of the proximal end resulted in the decrease of the systemic blood pressure in all cases. The eye pressure decreased in some and increased in others, i. e. a weak stimulation resulted

in the lowering of the eye pressure in most of the animals, but a strong stimulation caused an elevation of the eye pressure, mydriasis and systemic spasm in every case.

Electric stimulation at the distal end of the nerve. The stimulation on the distal end resulted in no change of the intraocular and the systemic blood pressures and the width of pupils.

2) The influences of the ophthalmic nerve on consensual ophthalmotonic reaction.

The author has previously demonstrated, that when the intraocular pressure of one eye has been raised by the mechanical compression, the eye pressure of the other eye in contrast has fallen. In the present experiment it was proven that when the ophthalmic nerve has previously been cut on one side, the consensual reaction on the other eye as stated above did not appear. These results suggest, that the trigeminal nerve may be the afferent pathway of the autonomic adjustment reflex of eye pressure.

3) Influences of the trigeminal nerve on the eye pressure changes caused by ligation of the vortex vein.

The ligation of the vortex vein of a normal rabbit brought about a rapid elevation of the eye pressure, but after a while the eye pressure began to descend and on the following day it was found to have fallen below the initial level. Subsequently, however, the eye pressure began to ascend again gradually and finally reached the initial level within two weeks without passing beyond the normal level. While in the rabbits with their ophthalmic nerves cut, the fluctuation of eye pressure took a greatly different pattern from those of the normal, i. e. the fluctuation of the former was more extensive than that of the latter, and yet the subsequent elevation of the eye pressure did not stop at the initial level but rose passing far beyond it.

Conclusion

From the results of various experiments in an attempt to investigate the relationship between the intraocular pressure and the ophthalmic nerve, the author has come to the conclusion, that the ophthalmic nerve is one of the afferent pathways transmitting the various impulses caused by the changes in the intraocular pressure to the autonomic eye-pressure center, and the impulses created by these stimuli in the eye-pressure center are in turn transmitted to the eyeball by way of the autonomic nerves and thus the eye-pressure is autonomically regulated by these reflexes.

II. The effector organs in the eyeball

Little is known as regards to what part within the eyeball the impulse from the eye-pressure center is transmitted and what changes the impulse might bring about within the eyeball. Of many regional factors that exert influences on the eye pressure, some of the most important ones are are as follows:

1. The amount of intraocular contents: namely, the amount of blood in the intraocular vessels and aqueous humor, and the volume of lens crystalline, vitrous,

uvea, and retina.

2. Elasticity of the eyeball wall.

Of these, the most variable and most influential on the eye pressure are blood circulation and aqueous humor in the eyeball, and in addition the two have an intimate correlation with each other.

Elwyn[21] has picked the following three units as the effector organs for the maintenance of normal intraocular eye pressure:

1) The capillary walls and walls of Schlemm's canal.

2) The amount of circulating aqueous humor.

3) The amount of circulating blood.

The investigators upholding the neurovascular theory, Duke-Elder being the representative, have pointed out vascular disturbances within the eye as the cause of glaucoma.

Observations

As is clear from these, since the blood vessel system in the eye seems to have a very close relationship with eye pressure, the author has first investigated the blood vessels in the eye, uveal vessels in particular.

Distribution of uveal vessels[22]. The eyeball of the rabbit previously injected intravascularly with indian ink had been enucleated and made transparent using xylol or winter green oil, after fixing with formol, a study on the distribution of blood vessels in the eye was carried out.

Of the results, the most interesting find is the distribution of the choroidal vessels. Namely, choroidal vessels are found quite abundantly, and especially their veins are numerous and their tubular space much larger and their anastomoses more numerous than those of arteries. In addition, their capillary space is big, presenting the form that looks like a sinus as well as close-knitted meshes.

The finding especially noteworthy, is the relation of positions between the vascular layer and the capillary layer; i. e. the two are not located on the same plane but they are joined by the junctions branching out at right angle. Such a structure of the distribution resembles that of the liver and pancreas; and moreover, it is convenient for the passive retention of blood as well as suitable for the adjustment of the influences of systemic blood pressure, alleviating as much as possible these influences, acting as it does as a sort of buffer. Both the afferent and the efferent vessels of ciliary vessels are quite slender but the capillaries in between the two, have a markedly big tubular space as well as abundant anastomoses. As the rate of the blood flow at this area is quite slow, ciliary vessels seem, by virtue of their very structure, to be well suited for the circulating substances to permeate. In contrast to this, vessels of the iris are not suitable for blood retention or for the permeation of substances as both their tubular space and number are small.

Innervation in the uvea[23]. Of the workers who have investigated neural regulators

of the intraocular pressure, there are Lauber[24], Schaly, Löwenstein[25], Kiss[26], Orbán[27], and Ashton[28].

The author has traced the routes of nerve fibers by staining the uvea of the albino rabbit with Gross-Schiltze's, and Kultschitzky's stainings, and has investigated the relationship between the routes and vessels, reaching the following results:

Thd innervation in the choroid is quite abundant; and especially around its arterial branches, a dense and abundant nerve plexus is found; and at the distal end of its nerve fibers, Stoer's so-called "Terminal Reticulum" is formed and their ends are connected with the muscle fibers of the arterial vessel wall.

The innervation of venous branches is relatively less abundant but the nerves are likewise connected around these branches in a network form with an occasional "Terminal Reticulum". In the ciliary body and iris, the innervation for main blood vessels is not quite so compact but shows a simple communication of nerve fibers; and no "Terminal Reticulum" can be found. At the roots of the ciliary processes, however, a network of nerve fibers is formed, and this network seems to possess neural functions to control the aqueous production. Moreover, occasional ganglion cells can be recognized in the choroid.

From these experimental findings the following assumption may be made:

Those autonomic nerves entering into the choroid are mainly attached around arterial branches, and they perform the neural control over the rate of circulation and over the amount of blood; and in addition some are connected around venous branches, performing likewise a neural control. In the ciliary body, however, the autonomic nerve seems more likely to play a regulating role on the aqueous production, consequently adjusting the intraocular pressure. The choroidal veins also seem to play an important role in the adjustment of the eye pressure by their passive dilatation and contraction.

Functions of the ciliary muscles[11]. There are two or three investigators who support the opinion that the ciliary muscles, involved as they are in the outflow of the aqueous humor play a role in the adjustment of the intraocular pressure (Fortin[29], Stieve[30], and Thiel[31]).

The author, by using normal human eyes with theier pigments decolorized, studied the anatomical relation of ciliary muscles with other parts, and it has been demonstrated that the anterior ends of the meridional fibers of the ciliary muscles are connected with the scleral spur while their posterior ends reach both the elastic and the collagen fibers of the choroid. These findings seem to suggest that the contraction of ciliary muscles brings about a decrease in the intraocular pressure by accelerating the aqueous outflow, as well as by forcing blood out of the choroid. In fact, the author has been able to confirm, by the tonography that the accommodation actually accelerates the aqueous outflow.

Conclusion

From these experimental results, the author has reached the following conclusion:

The choroid possesses abundant blood vessels, and inasmuch as they carry a large amount of blood on account of their large tubular space, they also have such structural formation as to enable their distension or contraction greatly to influence the volume of intraocular contents. Moreover, as the autonomic nerves distributed in the eye are connected with the wall of vessels in a compact network of nerve fibers, the width of the choroidal vessels can be regulated by the autonomic center; and thus the intraocular pressure seems to be regulated by an increase or a decrease in the amount of intraocular circulating blood. On the other hand, the ciliary body likewise seems to take a part in the adjustment of the eye pressure as the width of vessels, the permeability of blood vessel walls, and the aqueous production are all controlled by the autonomic nerve, and because the contraction of ciliary muscles, as already mentioned, also exerts a great influence on the intraocular pressure.

Therefore, the author believes that a regional adjustment of eye pressure is being performed by these mechanisms, working as they are in conjunction with each other, and maintaining a harmonious relation among themselves under the control of the autonomic center.

Summary

From the results of the various experiments, the author has arrived at a conclusion that the intraocular pressure like the respiration, the blood pressures, the body temperatur, and so on, is adjusted autonomically; and has elucidated the mechanisms of these autonomic adjustment functions: namely, the intraocular pressure is managed and controlled by the eye pressure center located at the diencephalon and if any abnormal change of the intraocular pressure should occur, the resultant stimuli are transmitted to the eye pressure center via the ophthalmic nerve, causing an excitation of the center.

The impulse created in the center by these stimuli are in turn relayed to the eyeball by way of the autonomic nerve; and by inducing distension or contraction of uveal vessels, a rise or a fall of the blood pressure in ciliary veins, regulating the volume of the aqueous humor produced, and distending or contracting Schlemm's canal, the volume of intraocular blood and the quantity of aqueous humor are adjusted in the eyeball. By these, the intraocular pressure is thought to be adjusted automatically.

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ON THE INTERRELATIONSHIP BETWEEN BLOOD CHARACTER AND OCULAR PRESSURE IN GLAUCOMATOUS PATIENTS

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Introduction

Through the chemotherapy of glaucoma by means of " Diamox ", the suggestion that bicarbonate would play a significant role in the formation of aqueous humor was further confirmed. Then many works were carried out to clarify the mechanism of the circulation of aqueous humor and the etiology of glaucoma. The author also has been investigating the chemoterapy of glaucoma by means of Diamox for past three years. This report concerns the recent investigations along these lines.

Results and Conclusions

Diamox was administered to twenty patients with various types of glaucomas and effects of Diamox on various symptoms associated with glaucoma were studied. Recovery of sight, recovery from the contracted visual field, alleviation or disappearance

of such subjective symptoms as headache, nausea and halos as well as a lowering of the ocular pressure were observed in the majority of the patients tested. But a few patients showed marked symptoms of glaucoma without high ocular pressure while there were also such patients whose ocular pressure was not markedly lowered, no matter how significantly other various symptoms were alleviated by the administration of Diamox. Therefore, it is conceivable that the administration of Diamox could not result in the parallel recovery from various symptoms of glaucoma.

The erythrocyte sedimentation rate (E.S.R.) of glaucomatous patients was found to be higher than that of normal subjects. A normal E.S.R. was increased notably by adding both atropin and bicarbonate, but little, if any, increase was obsersed with atropin alone. On the contrary, even sole addition of atropin resulted in remarkable increase in E.S.R. of glaucomatous patients. Moreover, following the administration of Diamox, the erythrocyte sedimentation rate of glaucomatous patients was observed to show the similar tendency in that of normal persons.

From these results, it was suggested that the content of bicarbonate in the blood of glaucomatous patients might be higher than that of normal ones (2). This was confirmed by the determination of bicarbonate in the blood of patients with simple glaucoma with the aid of Warburg and Van Slyke apparatuses. The activity of carbonic anhydrase in the blood was lowered by the administrations of Diamox. However, any difference could not be detected between normal subjects and glaucomatous patients (3)(4). Bicarbonate or carbon dioxide in the blood of glaucomatous patients might play a significant role, but is yet obscured.

The following experiments were also carried out. Various materials such as air, oxygen, carbon dioxide gas, distilled water and a sodium bicarbonate solution were injected into the anterior chamber of rabbits' eyes, and changes in intraocular pressure were observed manometrically. As shown in Fig. 1, both CO_2 and sodium bicarbonate

Fig. 1 CO_2 0.1cc.

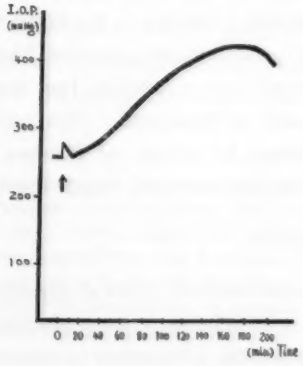


Fig. 2 N/72 H_2SO_4 pH2.4 0.05cc

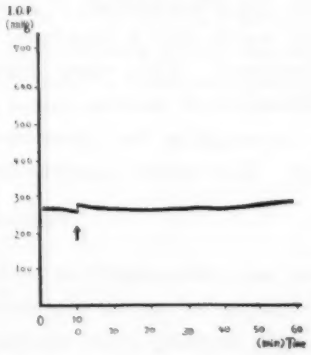


Fig. 3 N/48 H_2SO_4
pH1.4 0.05cc

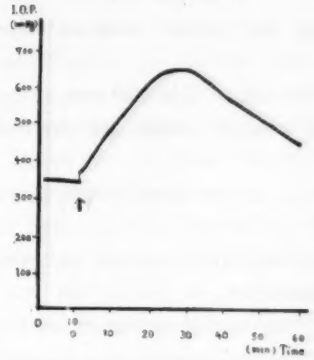


Fig. 4 N/500 NaOH
pH8.0 0.05cc

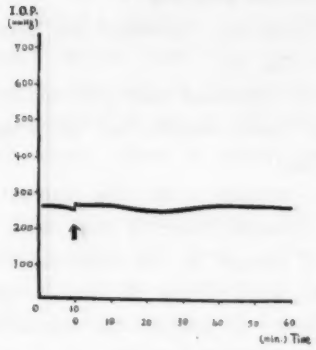


Fig. 5 N/400 NaOH
pH8.0 0.5cc

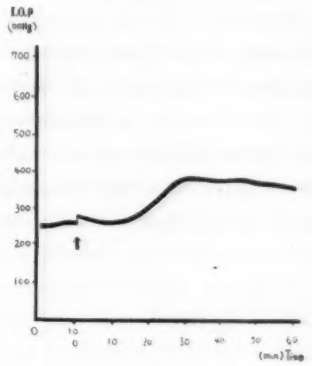
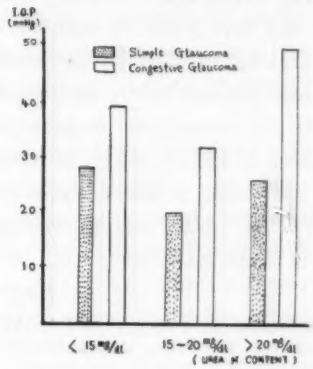


Fig. 6 The relationship between blood urea content and i.o.p.



solution caused a rise in intraocular pressure, but the remaining three did not show such an effect (5). Further, an intracameral injection of ascorbic acid or lactic acid solution also caused an ascent in intraocular pressure. But in this case pH of the solutions had to be considered. As shown in Figs. 2,3,4, and 5, in case of H_2SO_4 or NaOH injection, a rise in intraocular presssure was observed when pH of the injected solution was lower than 2.0 or higher than 8.5. (6).

Determination of N.P.N. in the blood was carried out in twenty three patients with simple glaucoma. It was demonstrated that the content of N.P.N. in the blood was higher than that of normal ones, and that the higher content of N.P.N. was remarkably reduced by the Diamox administration (7).

Further, blood urea and amino acid nitrogen levels were comparatively studied in 35 glaucomatous patients and 19 normal subjects with the following results:

1) The blood urea content of glaucomatous patients was significantly higher than that of normal subjects.

2) Proportion between the urea content and the ocular pressure failed to be detected (Fig. 6).

3) No difference was observed in the content of amino acid nitrogen (8).

From these results, the following two points must be considered for the etiology of glaucoma:

1) A change in the total amonut of bicarbonate in the blood which is associated with the dynamic state of body salts.

2) A change in the mechanism of the urea formation and/or its excretion by which the total amount of urea in the blood is controlled.

In order to analyse the interaction between the ocular pressure and the urea formation, an effect of intravenous arginine on intraocular pressure was studied. Fifteen rabbits were injected intravenously with an arginine-HCl solution (500 mg./kg. body weight) and a tendency towards lowering of the ocular pressure (−4.5mm.Hg) was observed, but this action of arginine was temporary (9).

The contents of chloride and bicarbonate in the blood were determined in thirteen glaucomatous patients before and after the administration of Diamox. Marked increase in chloride and remarkable decrease in bicarbonate were detected in all cases (10).

An effect of DOCA, which is recognized as a controller of the dynamic state of body salts, on the ocular pressure was also studied, and a daily intramuscular injection of DOCA (1-5 mg.) into rabbits was observed to cause on occasional rise in intraocular pressure in some cases (11).

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ON THIRTY-TWO CRANIOTOMIZED CASES OF LEBER'S DISEASE WITH REFERENCE TO ITS GENETIC PROBLEMS

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Hereditary optic atrophy or Leber's disease, which is commonly assumed as a sex-linked, recessive, hereditary disease, nearly always begins with sudden impairment

of vision, reaches its worst in one or two weeks, and though slight improvement of vision occurs afterwards, is characterized its final stage by marked optic atrophy, central scotoma and impairment of vision. In 1943 at a meeting of the Kyoto Ophthalmologic Society Jo Imachi, one of the authors, stated from the results of his investigation of a family line, tainted with this disease as well as of his studies, one its onset, progress, spinal fluid findings etc. that arachnoiditis lay at the root of this disease. Later on in Japan too, Ken Imachi and others came to apply craniotomy to the therapy of this disease.

Since 1945 we have conducted craniotomy on thirty-two cases clearly confirmed as Leber's disease by the family-history investigation. With all these cases marked opacity and thickening of the arachnoid, and thereby-caused collection of the spinal fluid were noted not only at the chiasm, but widely on the surface of the cerebrum. We have already published several papers dealing with the family histories, therapeutic effects, histologic findings and natural cures of some of these cases. In particular our efforts in this line of research were rewarded by the discovery of two new facts, that is, the presence in the arachnoid tissue of thickened, hyalinized capillary walls, besides intensely proliferated endothelial cells and connective tissues, and the existence of cases which had completely recovered a visual function in spite of deadly pallor of their nerve-heads.

Further we investigated twenty-three families to which these thirty-two craniotomized cases (29 males and 3 females) belonged, and found 119 victims of the disease. With these patients male and female percentages, circumstances of onset, issues and effects of the craniotomy were studied with the result, that remarkable differences were found on these points between the male and female. As a few other hitherto-unnoticed facts have also been brought to light, we want in this paper to discuss, though briefly, the genetic problems of Leber's disease as well.

Cases and Discussion

Investigated Family Lines. One hundred nineteen patients taken up in this paper came from twenty-three tainted families with more than two diseased members.

As shown in Table I, the proportion of female cases to male ones was 56.6%, while as to craniotomized cases it was only less than 10%. This comparatively small number of craniotomized female cases may have been due, as will be explained later, to the fact that females patients generally possessed better stationary visions.

Difference in Age at Onset between the Male and the Female. Eighty cases (56 males

Table I

Male cases	76	Female cases	43	Total	119
Craniotomized Male cases	29	Craniotomized Female cases	3	Total	32

Table II Difference in Age at onset between the Male and the Female

Ages at onset	Male	%	female	%	Total	%
5～9	3	5.39	0	0	3	3.75
10～14	11	19.61	6	25.25	17	21.25
15～19	23	41.05	9	37.5	32	40.0
20～24	15	26.75	4	16.67	19	23.75
25～29	4	7.15	1	4.17	5	6.25
30～34	0	0	1	4.17	1	1.25
35～39	0	0	1	4.17	1	1.25
40～44	0	0	1	4.17	1	1.25
45～49	0	0	0	0	0	0
50～	0	0	1	4.17	1	1.25
	56		24		80	

Table III Comparison on Stationary visual power between the Male and the Female

Stationary visual power	Male eyes			Female eyes		
			%			%
0～0.01	30	39.42		3	10.71	
0.02～0.03	17	22.35		7	25.0	
0.04～0.05	8	10.52	80.26	0	0	42.84
0.06～0.07	4	5.26	89.43	1	3.57	60.91
0.08～0.07	2	2.63		1	3.57	
0.1	7	9.21		5	17.85	
0.2	1	1.32		2	7.14	
0.3	4	5.26		0	0	
0.4	0	0		2	7.14	
0.5	1	1.32		1	3.57	
0.6	0	0		0	0	
0.7	0	0		1	3.57	
0.8	0	0		0	0	
0.9	0	0		0	0	
1.0	2	2.63		3	10.73	
1.2	0	0		2	7.14	
	76			28		

and 24 females) whose ages at the onset of the disease had been ascertained were selected from 119 cases and given in Table II.

As shown in Table II, the onset of the diseases was most frequent in the age group of 15 to 19, though according to other reports the disease most often attacks a little younger persons. Generally-speaking, female cases were affected later in years than male ones. Three males cases had the symptoms of the disease already at the age of less than nine years, while there was no male case affected after the age of thirty. On the other hand every female cases remained unaffected till the age of ten.

while the percentage of those affected after the age of thirty was as high as 17. We know of one female case who suffered from an acute attack after the age of fifty, and later showed simple optic atrophy.

Difference in Stationary Visual Power between the Male and the Female. Seventy-six male eyes and 28 femal eyes, all with optic atrophy and settled symptoms, were picked up from 119 cases and tabulated according to their respective visual powers in Table III.

All the eyes included in Table III were those which had long been subjected to medical treatments and no longer showed any sign of improvement or deterioration. Ninety percent of male eyes were those whose stationary vision was less than 0.1, and even those with the vision of less than 0.01 occupied 40%. On the contrary on the female side the percentage of the eyes whose stationary vision was less than 0.01 was as low as 10.7, and that of those with the vision of less than 0.1, 60.7. Moreover there were five female eyes (18%) which gave the vision better than 1.0 in spite of their pale discs, while the vision better than 0.2 had been restored back to 40% of female eyes. This fact may be taken as an explanation for the smaller number of female patients who wish to be operated on.

It is noted that the incidence among women of Leber's disease is much higher in Japan than in Western countries. Our investigations, however revealed, that women were generally affected more lightly and at a higher age than men, and that they were were more responsive to ordinary symptomatic treatments, and more liable to natural recovery. This fact becomes really conspicuous, when male and female scions of the same family are affected and treated in the same way. Male members of the S. and W. Families whose discs were quite white had the much reduced vision of 1m./FC, and did not mend at all, while their respective sisters who likewise in the past had experienced severe impairment of vision and other symptoms of acute optic postneuritis, got well in the course of time, and regained the normal vision of 1.0, though their nerve-heads too showed the appearance of simple atrophy. As for craniotomized cases, a female member of the N. Family in Kochi Prefecture had the vision of 1.0 restored back a year after craniotomy, but her equally surgically-treated brother left hospital with the vision of 0.2, despairing of further recovery.

Such a comparison on the prognosis of Leber's disease between the male and the female as given above is, we presume to think, the first of its kind on medical record.

Exposure of the Chiasm and Recovery of Visual Power. In 1912 Cushing detected brain edema in Leber's disease, and in 1931 Kuhn surgically treated a case of this disease by exposing the chiasm, where he noted proliferation of fibrous tissues and light inflammatory infiltration. He reported, that a surgical operation produced temporary curative effects which were nullified by aggravation a few months after. In 1939 Hermann followed suit, Puech, Bonnet and Guillaumat in 1940, and Rubino in 1941. Worthy of special attention is that Puech thereby restored the vision of 1/50 to 10/10.

In 1942 Jo Imachi had the opportunity to examine two patients with Leber's disease, a brother and his sister. They were respectively the eighth of ten children. The first, second and third children contracted a brainsickness at the age of four or five years, and were paralyzed and unable to stand on their feet, died four or five months after. The fifth child lost eyesight at the age of 12 and was diagnosed as a case of simple optic atrophy. At the age of 17 he too died of a brainsickness in fever and convulsion. The seventh child was a lad of 25 years old when examined. He said he had lost eyesight at the age of 12. His discs being fallen into simple atrophy, he could barely count fingers before the eyes at the time of examination. As for the eighth one, when she was 21 years old, and in the third month of pregnancy, she first noted central scotoma in her left eye, which was judged as due to optic atrophy. Nine months after delivery the same symptom appeared in the right eye, which, when examined, was found to be presenting the picture of optic neuritis. The vision of the right eye was 0.5, and that of the left 0.01. Every day Imachi carefully conducted perimetry and scotometry, and found daily fluctuations in the results. And as he also took note that the patient has a headache, he concluded that the chiasmal arachnoid was involved in Leber's disease, and in 1943 asserted for the first time in Japan, that this hereditary disease should indicate craniotomy. In the same year the first craniotomy for Leber's disease in Japan was performed by Ken Imachi. The lead thus given was soon followed by Jo Imachi, Ichizo Yaso, Shuichi Matsumoto and others. Up till now, Ken Imachi has reported on ten operated cases, and we, Jo Imachi and his

Table IV Comparison Between visions before and after Craniotomy for Leber's Disease

Visual powers	Preoperational eyes	%		Postoperational eyes	%	
~0.01	22	37.9		4	6.9	
0.02~0.03	17	29.3		10	17.4	
0.04~0.05	5	8.6		17	29.3	
0.06~0.07	3	5.17		2	3.44	
0.08~0.09	2	3.44		2	3.44	
0.1	4	6.9	15.5	8	13.76	39.7
0.2	0	0		2	3.44	
0.3	1	1.72		0	0	
0.4	0	0		1	1.72	
0.5	1	1.72		4	6.9	
0.6	0	0	8.63	0	0	25.85
0.7	0	0		2	3.44	
0.8	0	0		0	0	
0.9	0	0		2	3.44	
1.0	1	1.72		0	0	
1.2	2	3.44		4	6.9	
	58			58		

assistants, on 15 which belonged to nine tainted families. As our operated cases have meanwhile amounted to 32, we are now in a position to be able to make a fair assessment of the curative value of craniotomy. Table IV shows improvement through operation of visual powers. Listed in the table were only 58 eyes whose visions could be examine some long time after operation.

As shown in the table, only 8.63% of 58 eyes had the vision better than 0.2 before craniotomy, but after it as many as 26%. As for the percentage of those with the vision better than 0.1, it increased through craniotomy from 15.5 to 40. Conversely the number of the eyes with the vision worse than 1.01 dwindled from 22 to 4. These figures are clear evidence of the curative value of craniotomy, which therefore may be said to be the sole and best remedy for Leber's disease under the present circumstances.

We formerly published a paper on arachnoid pathology in the Rinsho-ganka (vol. 8, P. 161-), and then in the Gankarinsho-iho (vol. 48, P. 451-) discussed the genetics, complications, and causative factors of this disease. The main points of our, these two former papers were something like this: in Leber's disease involvement of the arachnoid is not confined to the chiasm alone, as Ken Imachi et al. once maintained, but spread very widely on the frontal lobe surface. Over the entire arachnoid membrane are more or less clearly observable opacities, circum angio infiltration, proliferated thickened tissues, and nuclear swelling and vacuolization. Particularly at the chiasm circulation of the spinal fluid is disturbed on account of the abovementioned lesions, and moreover the hyalinization of capillary walls, formation of fibrin-plate thrombi, and fibrous exsudation from the vessels take place. Such involvement of the arachnoid may be looked upon as tissue allergy caused by some toxin. And fever of unknown origin, common cold and pregnancy are to be included among causative factors. In the present investigation too, thickening of the chiasmal arachnoid, and circulation disturbance of the spinal fluid were noted in all the cases. It was by tearing-off of arachnoid adhesion alone that a cure was effected.

Genetic Problems of Leber's Disease. Leber's disease has long been regarded as a sex-linked recessive hereditary disease, but unlike colour-blindness it is very rare.

Table V Difference in the Incidence of Leber's Disease between the Male and the Female %

	Male cases	Female cases	%	Conductors sick D-R Alteration	Conductors	%
Germany	300	25	8.4	114	4	3.5%
England	111	25	21.6	91	18	19.8
France	75	15	20.6	42	5	11.9
JAPAN (KAWAKAMI)	134	94	70	70	21	30.0
J. Imachi et al.	76	43	56.6	61	26	42.0

And so, if it were really sex-linked and recessively transmitted, there would be, as a natural consequence, nearly no female patient. The fact is, that a considerable portion of sufferers of this disease has always consisted of women since Hermuth's statistics. To make matters more complicated, the statistics from different countries differ widely from each other on the proportion of female patients to male ones. In Table V our statistics are shown along with those of other investigators.

As shown in the table, the proportion of female cases to male ones was 70% in Kawakami's statistics, while in Germany it was only 8%. Only four of 114 German conductors, that is, 3.5% fell sick, while the disease attacked 30%, according to Kawakami, and 42.6%, according to our investigatisn, of Japanese conductors. These figures seem really baffling to any genetic approach.

In 1924 Kawakami advanced D-R alteration theory in order to explain the high percentage of female patients in Japan. Waardenburg too wrote about the same time that it was quite possible for a woman with a heterozygote to fall sick. Meyer-Riemsloh evolved a similar view independently. According to Kawakami's explanation, a pair of hereditary factors, D and R, which are antagonistic to each other maintain a sort of balance of power between them, and if this balance of power is broken, under the influence of another hereditary factor, G, Disease Factor R gets the upper hand of Health Factor D. To fit the theory to facts, he said, that this alteration rate racially differed. There are, however, strong objections to the assumption of racial differences in the alteration rate. In 1943 Gompachiro Yasuzumi, for the explanation of the smaller number of female patients, held, that the disease factor would become dominant in a homozygote, as it was contained in a common chromosome, and its opposite factor in a sex-chromosome.

In one of our previous papers we reported a case in which all the children of a sick conductor fell sick. In this case Leber's disease undeniably showed itself as a sex-linked dominant hereditary disease. On the other hand we find in the medical literature many cases of Leber's disease, of which fever, common cold, pregnancy, delivery and long lactation have to be regarded as causative factors. A short time ago we had a following case.

H.T., ♀, 26 years of age, native of Tokushima Prefecture. Hospitalized on July 4th, 1956. At the time of her first confinement in October, 1945, nothing was wrong with her eyes. Had her second child in July, 1954, and kept breast-feeding till August. 1955, when she noted the failing of her eyesight. Had recourse to cod-liver oil and tonics, but in vain. Also complained of headache. In the latter part of October was medically treated, but her eyes had now got so dimmed that she was unable to read even newspapers. In June, 1956 was diagnosed as a case of optic atrophy at a certain university hospital and referred to our clinic.

We examined her on June 20th, 1956. Worthy of special notice was, that she had

breast-fed her baby for two years. A general neurologic examination revealed nothing particular. The discs of her both eyes were quite white. The vision of the right eye was 1 m./FC, and that of the left 50 cm./FC, both being unimprovable with glasses. She had not enough visual acuity to read a chart for near vision. In the field of vision concentric contraction of 30 degrees was noted, and scotometry disclosed a racketform central scotoma. Her brother of 31 years old whose vision had begun to fail ten years ago was said to be a case of optic atrophy, but her family was free from consanguineous marriage. We diagnosed this case as lactation neuritis with suspicion of Leber's disease. On craniotomy arachnoiditis was found, and after operation improvement was noted in her vision and field of vision.

We have already learned the big role sex difference plays in Lebr's disease, and also noted that such environmental factors as pregnancy and breast-feeding exert much influence on the onset of the disease. Therefore we do not place much confidence in D-R alteration theory which takes into account only manifested cases of the disease, but ignores both causative and environmental factors and so-called latent patients.

Concerning the difference in the incidence of Leber's disease between the male and the female we sought an opinion of Dr. Taku Komai, an authority on genetics. He said to the following effect· "Recently the term 'D-R alteration' has been dropped from use because of its vague meaning, and instead of it 'unstability of penetration' is now used. As a female patient comes of a heterozygote, she is subject to many sorts of individual variations in penetration and manifestation." With regard to our environmental factors such as nutrition and others, he said, "The high percentage of female patients in Japan will genetically be explained. Genetic factors have certainly more importance, though it is not to be decided at once whether manifestation of the disease depends on one genetic factor, or on a more complicated genetic milieu, namely, the composite action of many genes." He concluded, "In short Leber's disease is one of the most difficult and interesting genetic problems of the present day, but a complete solution of this problem is not yet forthcoming."

However, if we consider the relation of near work with the development of hereditary myopia, the effects of gourmandism and epicurism on predisposition to diabetis mellitus, and further the participation of mental strain and labour in the onset of esential hypertension, we realize the great significance of environmental factors in clinical medicine. And so we dare state on Leber's disease that though susceptibility or abiotrophic character of the optic nerve is transmitted together with predisposition of the arachnoid to inflammation, the real manifestation or onset of the disease is dependent on such environmental factors as toxicosis, pregnancy, abnormal endocrine, various infectious agents and deficiency neuritis due to malnutrition and lactation. As to the transmission of predisposition to Leber's disease it is probable thatthat is done in accordance with Dr. Komai's so-called genetic milieu.

Conclusions

Leber's disease is a sex-linked hereditary disease, and in its appearance takes the form of acute or subacute optic postneuritis. In all of our 32 craniotomized cases not only chiasmal, but widely-spread arachnoiditis was demonstrated. Exposure of the chiasmal optic nerve was always attended with good results. In the clinical picture of this disease the marked difference was noted between the male and the female, that is, it was recognized that women generally have a milder attack, and that at a higher age than men, that female cases have more prospects of natural amelioration, and that operational results are also much better in them.

Leber's disease affects only those with predisposition, but environmental factors have much to do with its onset.

Our thanks are due to Dr. Taku Komai, professor emeritus of the Kyoto University for his valuable information on the genetic problems of Leber's disease.

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STUDIES ON ANTIGENICITY OF COMPONENTS OF THE LENS

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It is well-known that components of the lens have a strong organ specifity, and in addition they have the species specifity not in a strict sense. However, it has still remained undecided, why the antigenicity of lens-components show such specifities, and therefore it can be thought, that the solution of the problem may explain the substance of the endophthalmitis phaco-anaphylactica. Thus, at first, both proteins and polysaccharides, components of the lens, were investigated on their antigenicity and mutual synergetic actions.

Antigenicity of lens-proteins

The components of the lens were devided into two groups, soluble and insoluble, and their antigenicities were compared with each other.

Experimental materials. After mincing and homogenizing the fresh lens of a cattle, its components are separated by centrifuging (6000 r.p.m) into both parts of supernatant and residue. The former is deemed to be soluble protein, while the latter is washed with water several times, and if it does not prove the presence of protein by Sueyoshi's method, it is deemed to be insoluble matter chiefly containing lipoids, mucoproteins

and so forth.

Experimental method. Respectively a six per cent solution was made, (here, a percentage of insoluble proteins was calculated from nitrogen content estimated by Folin-method), and adult rabbits were sensitized three times, at intervals of two days, by dosing the solution of 3.0, 4.0 and 5.0 ml. respectively. A week after finishing sensitization, one ml. of one per cent solution was injected into the vitreous body of each rabbit, and then each response was observed.

Process of observation. The following tests and determinations were carried out.

(1) Number of leucocytes in blood. (2) Constituents of serum protein. (an increasing rate of γ-globulin) (3) Precipitin reaction on agar plate. (4) Protein content in aqueous humor. (5) Number of cells appearing in aqueous humor. (6) Histological picture. (7) Passive transference of sensitiveness. (8) Reaction in the cornea.

Results. According to the results of observation on (1), (2), (3), (4) and (6), it was recognized that an allergic reaction caused by soluble proteins is weaker than that by insoluble components. From the results on (5) and (6), a type of allergic reaction caused by soluble proteins was deemed to be of the "Arthus type". Especially, from the result of comparing soluble proteins with insoluble components in (7) and (8), it was assured, that the former's reaction is evidently "Arthus" and the latter's reaction is "Tuberculin" (Table 1,2). In the test (7), employing the method by Chase M.W., cell-components were taken with Tyrode solution out of the peritoneal cavity of rabbits and guinea pigs sensitized with soluble and insoluble components, and then those components were injected into the peritoneal cavity of a normal guinea pig. Two or three days later, their antigens were injected into the vitreous body respectively. The results proved, that the insoluble proteins cause notable ophthalmitis clinically as well as histologically, but the soluble protein can cause only a very weak inflammation

Table 1 Test of Passive Transference of Sensitiveness
(Landsteiner, K. & Chase, M.W.)

	Serum	Cell Component	Intracoreal Reaction	Judgement
Soluble Protein	+	−	−	Arthus Type
Non-soluble Protoin	−	+	+	Tuberculin Type

Table 2 Intracorneal Reaction
(Raffel, S. & Araund, L.F.)

	12 hours	24 hours	48 hours	Number of Cases	Judgement
Soluble Protein				7/8	−
Non-soluble Protein				7/8	+

which disappears within a short time. In the test (8), 0.02 ml. of 0.5 per cent soluble protein solution was injected into the cornea of sensitized guinea pigs, and a localized opacity, about 2 mm. wide, was made. The result indicated, that the allergic reaction is possible to occur in the cornea, avascular tissue, only when the insoluble components are injected, and results in the occurence of vascular invasion and the existence of remaining opacity.

Antigenicity of polysaccharides

Polysaccharides were extracted by the tryptic digestion method (Raistrick H. and Topley W.W.C.) from the lens capsule, and their antigenicity was investigated, 0.25-0.4 ml. of it a 0.1 per cent solution was injected intravenously into rabbits six times at intervals of two days in order to sensitize them, and the precipitin reaction and the skin tests were made of the sensitized rabbits. By comparing the results with the changes on the constituents of serum proteins and the histological finding, it was observed that polysaccharides in the lens can act as a complete antigen, at the same time when they have a strong toxicity.

Note. F.69/0 of lens-polysaccharide includes 8.72 per cent of nitrogen, 0.05 per cent of phosphorus, 28.8 per cent of reducing sugar and 4.5 per cent hexosamine, and shows the following reactions. sulfosalycylic acid (−), picric acid (−), biuret (±), Milon (−), ninhydrin (+), Molisch (卌), orcin (−), Fehling(+).

When a mixture of polysaccharides and lens-proteins is used to sensitize rabbits, it can cause the antibody production more rapidly than when the two are used separately, and moreover, the sensitization with a mixed solution can keep on the greater production of antibody content for polysaccharides during a longer period than the sensitization with polysaccharide alone. Besides, from the histological findings, it can be also recognized that the sensitization with a mixed solution causes stronger ophthalmitis, and at the same time it is accompanied by a delayed reaction

Sensitization with a slight amount of antigen.

It has already been well-known, that when the lens of one eye is injured, a part of its components becomes antigen, and the antigen causes ophthalmitis in the same eye, and sometimes it also causes the same symptoms in another eye. findings However such ophthalmitis is remarkably different in both the mechanism and the from the experimental ophthalmitis of sensitized animals. In order to solve this question, it was studied, whether the sensitization with a slight amount of antigen may cause the anaphylactic reaction, and as the result of experiment, the following facts became clear, at last it became possible to make a symptom quite resembling the human anaphylactic ophthalmitis.

After injecting only a slight amount of antigen (O.1 ml. of one per cent fresh lens-protein solution) into the anterior chamber of a rabbit, the production of antibody was not demonstrated in the skin reaction or the precipitin reaction, and also the

chang of serum protein was not demonstrated. A contusion was given to the eye right after injecting aqueous humor, and then its effects were examined. In this case, the skin reaction appeared evident about five days after giving the contusion, and the precipitin reaction, too, was observed about ten days after contusion. Besides, in constituents of serum proteins, the tendency of decreasing albumin and increasing β-and γ-globulin was assured. From those results, as it was supposed, that the existence of ocular inflammation plays an important part in the antibody production,

Table 3 Titration of Antibodies in Aqueous Humor of Sensitized Rabbits by Hanks' Method

Group		I			II			III	
No.	97	98	99	100	101	102	103	104	105
Serum	1:4	1:8	1:8	1:2	1:2	1:4	1:4	1:8	1:4
R Primary Aqueous		−			−			−	
R Secondary Aqueous		1:8			1:2			1:4	
L Primary Aqueous		1:1			−			−	
L Secondary Aqueous		1:8			1:2			1:4	

Table 4 Capillary Permeability Promoting Action of Serum Before and After the Provocative Injection

No.		C.P.P. Action		
		25×	50×	100×
9	Before	1×2	1×1	1×1
	After	10×2	10×10	10×10
10	Before	1×1	0×0	0×0
	After	8×9	8×8	8×8
11	Before	3×4	1×2	2×2
	After	8×9	10×12	10×10
12	Before	2×2	0×0	2×2
	After	10×11	11×12	10×10
13	Before	2×2	0×0	0×0
	After	5×6	3×5	5×5
14	Before	1×2	0×0	0×0
	After	6×8	4×8	4×4
15*	Before	1×1	0×0	0×0
	After	2×2	1×2	0×0
16*	Before	1×1	1×1	0×0
	After	2×2	1×1	1×1

*...Control plasma of previously not sensitized rabbits

the significance of ocular inflammation was further studied in various ways. Then it was observed that dropping acid on the eye and infusing iron salt solution are similarly effective to promote antibody production, but on the contrary, the antibody producing function is inhibited by the injection of china ink. Besides, the antibody production was also observed in case of sensitizing a rabbit with a slight amount of lens-proteins mixed with inflammatory aqueous (it has capillary permeability promoting action, which T. Kuroyanagi named so.). Moreover, the antibody production was observed as well in case of using rabbit-plasma, which had been activated with chloroform to display C.P.P. action. According to the facts above mentioned, it became clear that as the result of experimental inflammation, leucotaxine-like substance having C.P.P. action appears first in aqueous humor, capillary permeability and phagocytic action become active, and consequently antibody production is promoted. Finally, the influence of the intravenous injection of Shwartzman toxin on the antibody production was investigated. That is, one ml. pro kg of 1 : 20 culture filtrates of B. coli communior was injected into rabbits to cause the toxic ocular reaction, and then a slight amount of lens-protein was injected into the aqueous humor of one eye. In this case, ten days after injection, it was observed that a precipitin for lens-proteins appears in the aqueous humor of another eye and serum (Table 3). Besides, it was also observed that a strong ocular reaction occurs after the provocative injection, and several hours later, a total protein content in serum is decreased, γ-globulin is also decreased on paper-electrophresis, the number of leucocytes in the flowing blood is decreased, and then the fibrinolytic phenomenon (Macfarlane's modified method) and the promotion of capillary permeability (applying both methods of T. Kuroyangi's and H. Yanagida's) come out (Table 4).

It has been known, that it needs an intensive sensitization to cause the experimental anaphylactic ophthalmitis at a high rate. Guyer M.F. and Goto Y. employed a small amount of antigen in each experiment, but it seems to be very difficult. Burky E.L. using staphylococcus toxin, and Mueller H. and Maeda K. using Freund's adjuvant, tried to increase the antigenicity of the lens, and they published respectively a pretty good result. We noticed the report written by Ajo C., which showed that the toxic ocular reaction caused by Shwartzman's toxin can promote the capillary permeability of the ciliary body, and applying it we could succeed in promoting the antibody producing power of sensitized animals. It is conceivable that the promotion of capillary permeability of the ciliary body activates the absorption of antigen, and successively promotes antibody production. In other words, it is assured that the antigen injected into one eye does not directly flow into another eye as Schlaegel explained, but it can promote antibody production in the whole body, and consequently there appears an antibody in another eye. Accordingly, this explanation disagrees with Mueller H. who thought that an action of Shwartzman's filtrate depends on its combination with lens-proteins.

Conclusion

According to the facts above mentioned, the following results were obtained:

1. Concerning the antigenicity caused with lens-components, an action of insoluble proteins is much stronger than that of soluble proteins. The former has the "Arthus-type", but the latter rather shows "Tuberculin-type".

2. Lens-polysaccharides, too, have the antigenicity, and its action is promoted by the synergetic action with lens-protein. In this case, its histological picture is a mixture of an immediate type and a delayed type.

3. Even if a very small amount of lens-protein is employed, its antibody production is promoted by the toxic ocular reaction witn Shwartzman's filtrate.

4. Therefore, it seems to be possible to cause an experimental ophthalmitis quite resembling the human endophthalmitis phacoanaphylactica.

Finally, the names of collaborators in this work are as follows: Kishimoto, S., Suzue, S., Kizu, T., Kido, R., and Konishi, K.

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Editorial News

Distribution of Medical Schools in Japan

Name	Foundation	Adress
Hokkaido University Medical School	(n) 1922	Sapporo, Hokkaido
Sapporo University of Medicine	(m) 1950	Sapporo, Hokkaido
School of Medicine, Hirosaki University	(n) 1945	Sagara-cho, Hirosaki
Iwate Medical College	(p) 1928	Uchimaru, Morioka
Faculty of Medicine, Tohoku University	(n) 1889	Kitayoban-cho, Sendai
Fukushima Medical College	(m) 1944	Suginome-cho, Fukushima
School of Medicine, Gumma University	(n) 1944	Maebashi
Chiba University, School of Medicine	(n) 1882	Inohana-cho, Chiba
School of Medicine, University of Tokyo	(n) 1871	Hongo, Tokyo
Tokyo Jikei-Kai School of Medicine	(p) 1881	Atagomachi, Minato-ku, Tokyo
Tokyo Medical College	(p) 1916	Kashiwagi, Shinjuku-ku, Tokyo
School of Medicine, Keiō University	(p) 1920	Shinanomachi, Shinjuku-ku, Tokyo
Nippon Medical College	(p) 1924	Komagomesendagi-cho, Bunkyo-ku, Tokyo
Tokyo Women's Medical College	(p) 1924	Kawada-cho, Shinjuku-ku, Tokyo
School of Medicine, Tōhō University	(p) 1925	Omori, Ota-ku, Tokyo
School of Medicine, Nihon University	(p) 1927	Oyaguchimachi, Itabashi-ku, Tokyo
Shōwa Medical College	(p) 1928	Hiratsuka, Shinagawa-ku, Tokyo
Juntendō University Medical School	(p) 1943	Yushima, Bunkyo-ku, Tokyo
Tokyo Medical and Dental University	(n) 1944	Yushima, Bunkyo-ku, Tokyo
Yokohama University, School of Medicine	(m) 1944	Urafune-cho, Minami-ku, Yokohama
Niigata University, School of Medicine	(n) 1910	Asahimachi, Niigata
Ophthalmological Clinic, Shinshu University	(n) 1944	Asahimachi, Matsumoto
School of Medicine, Kanazawa University	(n) 1884	Tsuchitoriba-nagamachi, Kanazawa
Nagoya University, School of Medicine Institute of Environmental Medicine, Nagoya University	(n) 1882	Tsurumai-cho, Shōwa-ku, Nagoya Furocho, Chikusa-ku, Nagoya
Nagoya City University, School of Medicine	(m) 1943	Mizuhodōri, Mizuho-ku, Nagoya
Gifu Prefectural Medical School	(m) 1944	Tsukasamachi, Gifu
Faculty of Medicine, Prefectural University of Mie	(m) 1944	Sakaemachi, Tsu
Kyolto Prefectural Medical University	(m) 1884	Hirokōji, Kawaramachi, Kamigyo-ku, Kyoto
Faculty of Medcine, Kyoto University	(n) 1902	Kawaramachi-Shogoin, Sagyo-ku, Kyoto
Osaka University Medical School	(n) 1891	Dōjimahamadōri, Fukushima-ku, Osaka
Osaka Medical College	(p) 1929	Takatsuki-shi, Osaka
Kansai Medical College	(p) 1932	Moriguchi-shi, Osaka
Osaka City University Medical School	(m) 1945	Asahimachi, Abeno-ku, Osaka
Nara Medical College	(m) 1945	Kashihara
Wakayama Medical College	(m) 1947	7-Bancho, Wakayama

46 in all	national	(n)	20
	private	(p)	13
	municipal	(m)	13

Professor	Successive Professor
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Toshizo SUEYOSHI	
Kimiho IRINODA	
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SUBJECT INDEX TO VOLUME I

A Aqueous
outflow (Ohashi), 89
vein: in glaucoma problem (Kishimoto), 144
vein: in acute glaucoma (Ogino),171
ATP
of retina (Ezuka), 13
C Choline
of retina (Niwa), 155
Choroid
and sclera: pigment cells of (Igo), 124
Cornea(1)
epithelium: effects of denervation and stimulation of sympathetic and trigeminal nerve on mitotic rate of (Mishima), 65
nerves: embryological study (Kitano), 48
phosphate metabolism, using P^{32} (Fukado), 55
rabbits: fibrous structure and polarization optical properties (Kikkawa), 35
rabbits: thermoelasticity and submicroscopic structure (Kikkawa), 42
D Disease
Leber's: on thirty-two craniotomized cases of (Imachi), 236
E Electro-
myogram: of palsied extraocular and levator muscles (Kamouchi), 30
oculogram: clinical application of (Hiroishi), 194
Eye
diseases: statistical observation of eye clinic, university of Tokyo (Uchida), 179
pressure: autonomic adjustment function of normal eye (Akagi), 136, 225
vascular architecture of (Obara), 190
G Glaucoma
angle of anterior chamber and aqueous vein in acute (Ogino,) 171
appearance rate of ring of rainbow tints (Shimizu), 221
interrelationship between blood character and ocular pressure (Kinugasa), 233
L Lens
antigenicity of components of (Mizukawa), 244
Lymph
channels: in vitreous (Isayama), 208
M Maxwell's
Spot: clinical significance of (Urayama), 119
Myopia
genetic mechanism (Furusho), 185

N Nasolacrimal
duct: observation of opening of (Kuribayashi), 96
Nerve
ganglion cells in root of IIIrd, IVth, and VIth cranial (Fukuda), 60
O Ocular
changes: by shock stimuli (Nakaji), 214
uni-movement: objective measurement of limit of (Yamashiro), 130
P Phosphate
metabolism: of cornea with aid of radioautography, using P^{32} (Fukado), 55
R Retina
analisis of spatial summation of sensitivity of (Shikano), 1
cholin substance of (Niwa), 155
morphological study of pigment granules of (Takeuchi), 100
Retrolental fibroplasia
histopathological finding of (Hirose), 106
Riboflavin
in Behçet's syndrome (Eguchi), 22
S Syndrome
Behçet's: metabolism of riboflavin in (Eguchi), 22
T Trachoma
urogenital (Oishi), 83
Tumor
pituitary region: on operation "pernasal method" in (Takahashi), 159
V Visual
perception of moving objects (Asahi), 199
Vitreous
physico-chemical studies of (Sugiura), 7

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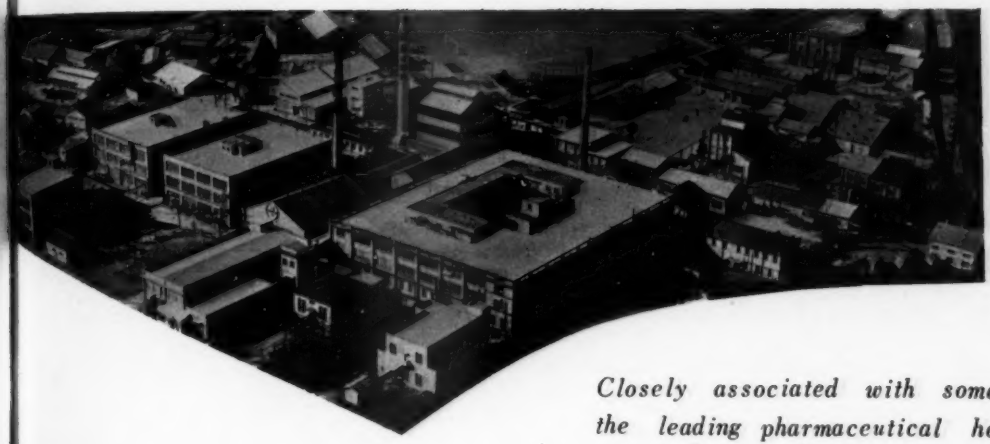

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